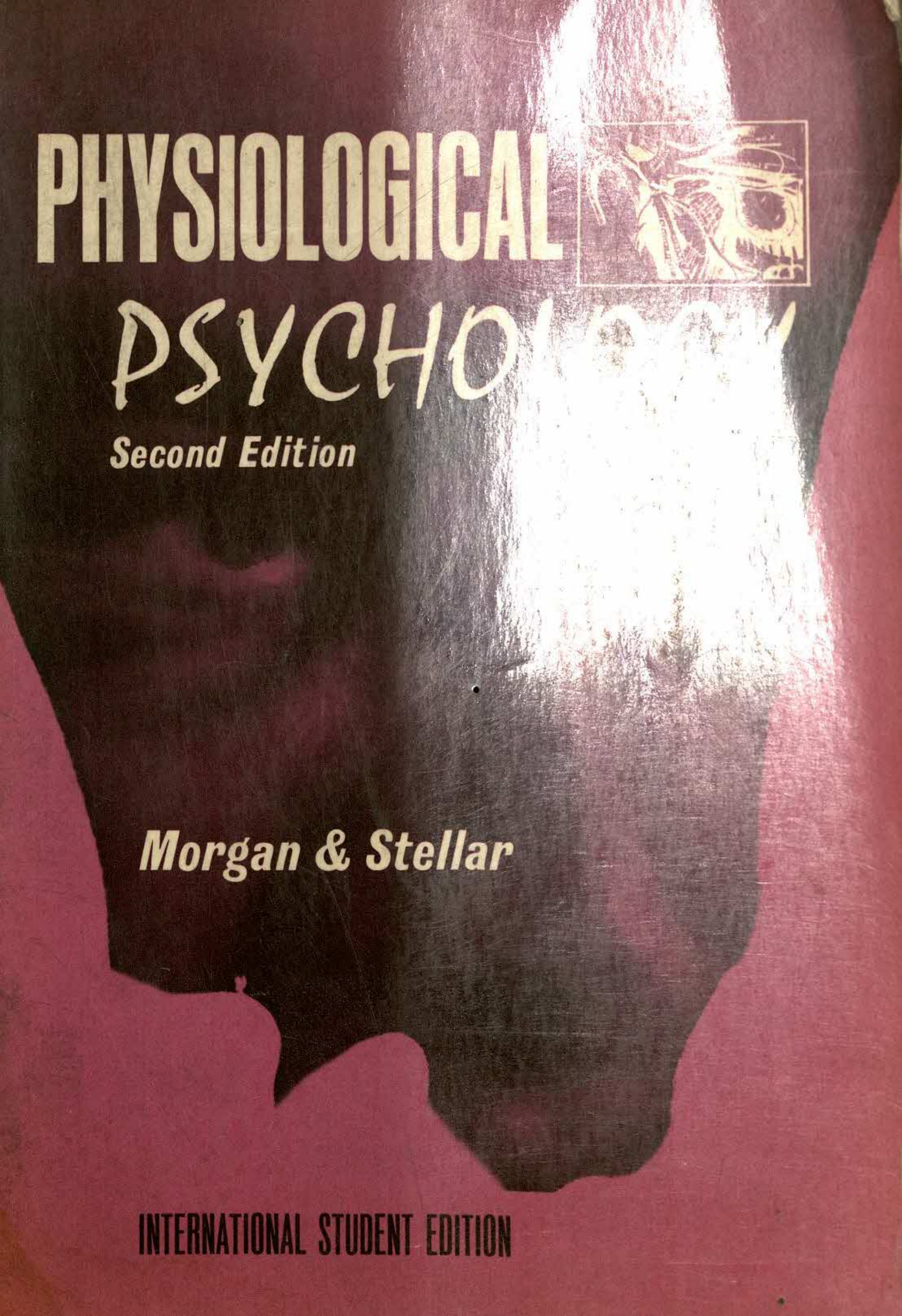

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PHYSIOLOGICAL PSYCHOLOGY

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PHYSIOLOGICAL PSYCHOLOGY

INTERNATIONAL STUDENT EDITION

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PREFACE TO THE SECOND EDITION

This book looks much the same in size and organization as the first edition, but there are really many differences. It is fair to say that this is a completely new edition, for almost every word has been written anew.

First of all, we have brought the book up to date. In the seven years since the first edition there have been many new developments and researches. We have combed the literature for them and woven the more important of them into the text.

Second, to make room for the new material we have had to drop some of the old. Sometimes that was easy to do, for the more recent research simply outmoded the old. In other cases it has been very difficult. In fact, we were forced to alter in two different ways our general policy on selecting content. One was to cut out summaries, discussions, and our own private theories about some problems. So we dropped the chapters on "Survey of the Senses" and "Survey of Adaptive Behavior." In other chapters, too, we cut down on theory, discussion, and summarizing. A second way of cutting down was to omit the more frankly psychophysical material. The reader will now find the treatment of such topics as brightness discrimination, dark adaptation, and loudness functions curtailed to make way for facts that bear more directly on the physiological basis of perception. Both policies were followed reluctantly, but we felt we had no other choice.

Third, it was inevitable that many minor changes in organization would come about with these additions and deletions of material. The order of the chapters on physiological background has been changed around to discuss the internal environment last rather than near the beginning. Two chapters on development have been dropped, but much of the material that was in them will be found here and there in other chapters. Because so much has happened in the field of vision since the first edition, a third chapter on color vision has been added. For similar reasons, three chapters instead of two are now given to motor functions. Learning has also been split into three chapters where there were two before. Two new chapters, "Behavior Disorders" and "Electrical Activity and Behavior," have been added at the end, although they cover some of the problems previously taken up in other chapters. There are also many changes in order and emphasis within each chapter.

In addition to these general points about the writing of the second edition, we want to acknowledge our debts, as best we can, to those who have helped us write it. John Spurbeck, Jewel Ann Fahy, and Charles H. Weber in our

Illustration Division have labored over the illustrations. James Gamble and Helene Kuhn typed the manuscript. Most of all, however, we thank Miss Kuhn for managing the whole process—the typing, the illustrating, the proofreading, and the indexing. She took the main burden of these matters off our shoulders and saw to it that they got done. Our wives deserve a lot of credit for their patience and encouragement through the long pull.

Finally, since two of us authored the second edition, we ought to say what we each did. Professor Stellar revised the four chapters on motivation: "Sleep and Activity," "Bodily Needs," "Mating Behavior," and "Instinctive Behavior." He wrote the new chapter on "Behavior Disorders" and the one on "Internal Environment," which has the same name as in the first edition but is really a new chapter. Professor Morgan has revised and written the other twenty chapters of the book and is fully responsible for them. Each of us has certainly made errors in the parts we have written, and we shall be grateful to the readers who will take the trouble to tell us about them.

CLIFFORD T. MORGAN
ELIOT STELLAR

BALTIMORE, MD.
April, 1950

FROM THE PREFACE TO THE FIRST EDITION

This book is meant to be both a textbook for undergraduates who are preparing for psychology or medicine and a reference book for graduate students and workers in psychology, physiology, and medicine. To serve this twofold purpose, the author has taken time to explain the elementary facts of psychology, physiology, and anatomy, and then has gone on to cover the more advanced aspects of research in the field, providing bibliographic references to the original papers used.

It was clear from the beginning that these two objectives could not be fully attained in every phase of physiological psychology, and therefore several principles were adopted in selecting the material to be taken up in the allotted space. The first principle embodied the conviction that the primary goal of physiological psychology is to establish the physiological mechanisms of normal human and animal behavior. On this principle several topics—for example, the effects of drugs and vitamin deficiency upon behavior—were not considered except as they are related directly to this goal.

The second principle was that the book should be factual and as free as possible from speculation and bias. Following this principle, experimental material obtained from animal studies has been emphasized at the expense of clinical observations on human individuals, for the animal experiments tend to provide more consistent and reliable information than do the clinical studies, which must in large part be based, unfortunately, upon subjective methods of observing behavior and upon accidental, often obscure, pathology. On this principle, too, the author has minimized "arm-chair" physiological psychology in which physiological mechanisms are deduced from purely psychological phenomena without corroborative evidence from physiology.

Nonetheless, the reader will find interpretation and theory given some place in the book. A definite point of view, even if not explicitly stated, is implied in the organization of material and in the manner of describing results. An attempt has been made, too, to point out the significance of results to show how they favor or argue against theories that have been proposed. In certain places, the interpretation of results does not agree with the authors who report them or with others who have made reference to them. In all cases, however, an endeavor has been made to separate facts and theories so that a reader, if he chooses, can reject a theory without denying the facts upon which it is based.

A third rule that has been followed concerns particularly the more sophisticated reader and experimenters in the field of physiological psychology. Since not every topic could be treated exhaustively, the exposition has been made most complete for topics that are not summarized in other readily available sources. For topics adequately considered elsewhere, the author has been content to present what seems to be a fair over-all picture of the material and to make sure to include the most recent and most significant studies. The same rule applies, also, in giving references to original papers. The listing of names and papers is not thorough where rather complete and up-to-date summaries of the literature already exist, as is the case in vision and hearing, but in other topics references are supplied for almost every statement. Furthermore, the rule is followed throughout that where there is a choice between references covering the same topic, the latest one is given. This rule, unfortunately, may occasionally have done injustice to the early and perhaps classic work of an author, but for the student who wishes to make use of the bibliography for more advanced work it should prove to be of advantage.

Two sorts of bibliographic references have been provided for the reader who wishes to do further reading on a topic or who would like to know the basis of the facts or conclusions that are presented. At the end of each chapter a few general references are given which cover topics considered in the chapter. At the end of the book is a bibliography of titles for specific points in the text. With each reference is an indication of the page in the text to which it applies. Thus the bibliography serves also as an author index. All names that appear in the text, whether within parentheses or not, refer to the general bibliography, not to the titles at the end of chapters. This system is used in order to provide a list of titles, particularly recent ones, in the field of psychology, without duplicating or dispersing titles among the various chapters.

The authors and publishers who have kindly permitted the use of their illustrations are acknowledged in the legends of the respective illustrations.

CLIFFORD T. MORGAN

CAMBRIDGE, MASS.
July, 1943

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CHAPTER I

INTRODUCTION

Our first task in a book like this is to define our subject and to tell you how we are going to go about it. This chapter will do that. First we will define "physiological psychology," then we will run over the outline of the book, pointing out its main problems and purposes, and at the end of this chapter we shall have something to say about the approaches and methods used in our subject.

Definition. *Physiological psychology* is not easy to spell, and many people are not very familiar with it. It is not hard to define, however. Physiology is the science of bodily functions; it has to do with the processes going on in the organs and tissues of the body. Psychology, on the other hand, is the science of behavior; in psychology we try to see how human beings and members of the animal kingdom adjust to the world they live in. Our task in physiological psychology is simply to put these subjects together and see how the physiological processes of the body are related to behavioral adjustments. That, in brief, is a general definition of our subject.

THE BOOK AND ITS PROBLEMS

In order to get a bird's-eye view of what is to come, let us go on to take up some of the general aspects of our subject. In fact, it will serve better to define physiological psychology and what it is about if we talk for a moment about the outline of the book and what it means. There are 25 chapters after this one, but these chapters fall into six main groups. Each group has a few central problems that run through almost all of its chapters. Let us see briefly what these problems are.

Physiological Backgrounds. The first group of chapters has to do with the physiology of the organism. Students of physiology would have to know their subject very well to have all the facts and concepts that we need for our task. Many of you who read and study this book will have had little or no physiology. So to provide the proper physiological background for both the expert and the novice, we have tried to pick out and organize as briefly as possible the high lights of physiology that we need to get on with the main problems of the book. When we say *physiology*, however, we speak loosely, for the next chapters have in them a lot that is outside the bounds of physiology. It would be more correct to say that they contain the basic anatomy, physiology, and biochemistry for studying physiological psychology.

The events in the body that we need to know about concern two main features of the body, the response mechanism and the internal environment. The response mechanism includes our various sense organs, our nerves, our nervous system, and the various muscles and glands that we use when we make responses. The internal environment, on the other hand, is the complex of substances—the food materials we take in, the secretions of our glands, the metabolic products of our body's functions—that move around the body in the blood and lymph and make up an essentially chemical environment for the nervous system and the response mechanism in general.

Of the four chapters on physiological background, three have to do with the response mechanism and a fourth with the internal environment. It is in the latter that we run into quite a lot of biochemistry. What we say about the response mechanism, however, is partly anatomical and partly physiological. In order to know how the body functions we must know how it is built, and that is particularly true of the response mechanism. So we take two chapters to describe the anatomy of this mechanism and its many parts, and then come to its physiology.

As we go along in the book we often introduce new facts about anatomy, physiology, or biochemistry as they are needed to deal with particular problems. The chapters of the first group, however, give the background needed to approach the other problems. With them behind us, moreover, we can outline the rest of the book in terms of the major problems of psychology, rather than those of the background sciences.

Sensory Functions. It is only in the second group of chapters that we start on the main problems of physiological psychology. This group concerns the senses. It is the largest group in the book, in terms both of number of chapters and number of pages. The reason for that is that we know more about the senses than we do about almost any other aspect of physiological psychology. The senses are accessible to our view, modern engineering has given us ways of making up and controlling the stimuli we use in studying them, and it turns out finally that the senses are easier to get to know than are other functions.

The senses give us good examples of the general approach we take in physiological psychology. First we must know pretty well the psychology of the senses, *i.e.*, how well man and animals can discriminate various kinds of sensory stimuli and how they perceive what goes on about them. Then we must gather all the facts we can about the sensory systems of the body, *i.e.*, how the sense organs are built, what sensory nerves connect with them, where these nerves go in the brain, what centers they serve there, and how these centers are affected by different conditions of the internal environment. Then we run experiments in which, for example, we see how removal of a particular visual center of the brain affects an animal's ability to see objects. Thus we find out how parts of the sensory system function in our perceptions. Later we shall see examples again and again of this sort of approach. Here we need only get the main idea.

When we sift away thousands of details and look for the main features of sensory functions, we come to four main attributes of sensation: intensity, quality, space, and time. These are the main aspects of our sensations for which we try to find underlying physiological events. A light seems bright or dim, a sound loud or faint, or a pain mild or strong—that is what we mean by intensity as an attribute. Our experience of various stimuli also has quality; some lights are red and others green, we hear tones of high pitch and low pitch, and we may feel a pinch on the arm as pain or simply pressure. These are all qualitative differences. In addition, we experience spatial aspects of stimuli. Visual objects, for example, have shape, size, distance, and location—all spatial aspects. Even sounds seem big or small, near or far away; and most stimuli that we sense with our skin have some size and shape. Finally, we also sense the time in which stimuli occur—whether it is long or short, intermittent or steady.

All four of these features of sensory experience are problems of physiological psychology. We shall have much to say about each of them. In each case we try to see what is going on in our brains and sense organs that accounts for the feature we experience. Of the four attributes of experience, quality is the one that has long been the baffling problem and the one getting a lot of attention. What is the physiological reason that we see red rather than green or hear a high tone rather than a low tone? We have countless experiments on this kind of question, and much that we have to say about the senses will bear on it. It will be a central problem when we come to the group of chapters about the senses.

Motor Functions. Each sense has its own sense organs and, to a large extent, its own pathways and centers in the nervous system. It is therefore easy to talk about each of the senses separately, as we have done in the separate chapters of the sensory group. There is not, however, any such simple division of motor functions, *i.e.*, of the ways in which we make movements and responses to our world. All the organs of response, including their centers and pathways, are so intimately linked together that it is hard to know how to deal with them and their functions in response.

What we have done is to make a group of four chapters, the first of which is strictly anatomical and physiological. It includes what the anatomists and neurophysiologists have been able to tell us about the organs of response. Following that there are three other chapters in the group that deal more specifically with motor functions. The distinction between them is not hard and fast, but it will do. One chapter, entitled "Reflexes," takes up the more or less automatic types of response that we call reflexes and postures. Another chapter deals with the less automatic and more highly coordinated responses of walking, running, swimming, and manipulation. In that chapter, called "Coordination," our problem is how the nervous system came to function so that we can do all these things. The final chapter of the group is "Emotion." It takes up the reactions that we think of as emotional and asks what goes on in the body and the brain to explain these reactions. Our problem in all these chapters is to trace out the mechanisms of our movements and patterns of response.

Motivation. Having finished with the sensory and motor functions, we go on in the next group of chapters to look at the physiological problems of motivation. The chapters in the group are entitled "Sleep and Activity," "Bodily Needs," "Instinctive Behavior" and "Mating Behavior." All of them describe kinds of behavior in man and animals that are not just responses to stimuli but are "driven" by some urge or drive within the organism. The problem is to find out what this drive is and how it works.

Many psychologists, especially those trying to construct theories of learning, have thought of drives as internal stimuli. Sometimes they are that, but as we shall see, they are usually more than that. Drives and basic motives, in fact, begin in our internal environment. This environment can affect the organs of the body in various ways. It can excite such receptors as those in our stomach, heart, or blood vessels, and these in turn can stimulate us to do something. Or it can directly excite some of the muscles of the body. Finally, and most important, it can directly excite some of the centers of the brain so that these centers bring out motivated behavior. There are in fact many physiological factors at work in motivation, and our problem will be to ferret them out and to piece them together into the picture that explains our basic motivations—for food, water, shelter, warmth, sex, and children. Those are some of the problems we shall take up in the chapters on motivation.

Learning and Memory. The fifth group of chapters has to do with learning and memory. In them we take up all sorts of learning from simple conditioned reactions to complex reasoning problems. Throughout these chapters run two closely related problems. One we might call the problem of localization: Are different sorts of learning and memory localized in particular parts of the nervous system? This is a very difficult problem, and we do not know as much about it as we would like to. We have, however, made some progress with it, and we know within limits what we can and cannot expect to find localized in the nervous system.

The other problem has many names and turns up in various places. It is the problem how one part of the nervous system can take over the functions of another part. When a person is paralyzed, *e.g.*, by a "stroke" (*i.e.*, a broken blood vessel in his brain), he usually improves over the course of time so that months after the injury he is much more able to use his arms than right after the injury. People sometimes forget many memories and habits after some part of their brain is injured, but they usually can get back the habits they lost by a little more practice—if the damage has not been too bad. These are just two examples of how the brain can manage to regain functions it has lost. This ability crops up in all sorts of learning and memory. Why it happens and how it happens is one of our chief problems in understanding how the brain and the body work in our learning and memory.

Man and His Disorders. The last group of chapters in the book does not fit into the pattern of earlier chapters. In fact, these chapters take up all over again some of the problems that went before. Their approach, however, is different. One chapter considers the whole problem of the functions of the brain in man, although it talks more about complex problems of memory than of sensory or motor functions. We call the chapter "Brain Lesions in Man," however, because almost all that we know about the brain and its function in man's behavior comes from cases of brain injury. Such cases have their shortcomings, as we shall see in the section below, and it is well to keep them in mind. A second chapter in the last group also emphasizes the more difficult problems of learning and intelligence in man but comes to them from a different point of view. It takes the various disorders of personality, learning, and intelligence that we find cropping up in human behavior and ties together whatever we can learn from such disorders about their physiological basis. The final chapter also cuts across the outline of earlier chapters. It takes up the ties between electrical activity and behavior. Although there are many places throughout the book where electrical matters are involved, it is only in the last chapter that we have an opportunity to consider the problem as a whole.

APPROACHES TO PHYSIOLOGICAL PSYCHOLOGY

That will give you a bird's-eye view of the book, its outline, and its problems. There are some other matters, however, that ought to be dealt with in an introduction. One is our general approach to our subject matter. It is well and good to say that we shall be concerned with the various physiological events that are linked with behavior. There are many possible approaches to this subject, and we cannot take them all. We should consider them, however, and explain which of them we will take.

Philosophic Approaches. To say that we are interested in the physiological events underlying behavior is just another way of saying that we shall talk about the problem of mind and body. This is as old as the ages. The founders of the world's religions, the philosophers, and almost all the intellects of the ages have had something to say about it. Some of their beliefs were well founded and forecast facts that have been proved in modern times. Some of their notions, *e.g.*, that the mentally ill are "possessed of demons," have proved very inadequate and in some cases dangerous to our society.

The important point, however, is not the belief but the way of arriving at it. Philosophers put forth their notions after they have read all they can of other philosophers and have seen all they can of the events that go on in the world. There is nothing wrong with this approach. For many problems in life, it is all that can be done, and it must be done. Luckily, however, the problems of mind and body have been lending themselves to scientific treatment. We do not need to rely on the opinions or conclusions of philosophers, no matter how well meaning or erudite. There are scientific facts with which to address most of the questions we can raise about the body and the mind.

Clinical Approaches. Another possible approach to physiological psychology is through clinical experience with sick people. Medical men see many cases of people who have some illness of the mind or the body or both. By taking in all they see of such patients and putting the facts together, they ought to be able to tell us something about mind and body and how they are related. They have. Medical clinicians, in fact, tell us about two main ways in which they find the mind and body—physiological and psychological processes—linked in sick patients.

One is the case of a person with an illness of the mind that causes a disorder of the body. Many people coming routinely to the medical practitioner have always been in this class. Only in the last few years, however, have we come to see how prevalent and how serious this kind of ailment can be. A branch of medicine—in fact, a specialty within psychiatry—known as *psychosomatic medicine* has grown up to deal with it. This will certainly come more and more to the fore in the years to come. Indeed it should help tell us more and more about the mind-body problem. At present, however, it is still young. It is very early to know what to make of much of the clinical material that is being collected. Moreover, we have little or no experimental backing for many of the ideas of psychosomatic medicine. The net result is that you will find little of them in this book. In years to come, however, the story may be different.

The other kind of clinical relation between mind and body is the case of people who have suffered some bodily illness which in turn affects their minds. Such illnesses have been carefully studied over the years, and they are some help to us. We have, for example, many cases of people who have had a tumor or injury to their brains. The effect of these injuries upon their behavior has told us a good deal about what the brain does in behavior. Similarly, we have clinical information about people with diseases of their glands, and this has pointed out how the glands function in intelligence and personality. In the book you will find a good many facts that have come from the clinical records of people with illness or injury.

We shall make good use of the clinical approach, but we should make it perfectly clear that the approach has its faults. In the first place, we are not always sure what is wrong with a patient. We may think he has a tumor of the brain when he has an infection, or more often we may believe he has a small tumor when he actually has a rather large one. Because we are not always sure just what is wrong, where it is, and how bad it is, we frequently cannot be sure what it is in the function of the body that makes a difference in behavior. Second, we usually cannot run what the experimental scientist calls "controls," *i.e.*, we cannot see what the patient's behavior was like when he was normal, and so we cannot always be sure that his physical illness is the cause of what seems to be a disorder of behavior. Third, we cannot get what we want to know when we want it. People get sick as nature decrees, and they very often do not have the kind of illness, at the time when we can make good use of it, to answer our scientific questions.

These are three principal difficulties with the clinical method. There are others, but it is not our purpose to criticize it. It is often the best that we have, and we should be glad to get it. We are going to use facts from the clinics in the book. Because of their drawbacks, however, we shall use them sparingly, and we shall try to sift the chaff from the wheat, bringing out the more important and more trustworthy conclusions one can get from the clinic, while leaving out or giving a back seat to the points that are in dispute or in doubt. Thus we shall give a place to the clinical method, but not the principal place.

Experimental Method. In clinical studies we so often would like to know what would have happened "if"—if the patient had a different illness, if he had a higher intelligence, if he had been brought up in a different family, if any one of a number of factors had been different. In history and the social sciences, the scholars would also give a great deal to know what would have happened "if—." Many of the sciences, however, particularly the natural sciences, do not work under the shadow of this big "if." They can find out, for they can *experiment*. They can set up the conditions just the way they want them, run their tests, and find out what lies behind the "if." It is largely for this reason that the natural sciences have made such great progress so rapidly.

Luckily, we can do experiments in physiological psychology. We do have our troubles, however. Animals and people do not always behave as docilely as machines do, and we must use our wits to set up just the kind of conditions we want. Our experiments are not nearly so neat and often not so clear-cut as they are in the natural sciences. But they are experiments, and they do answer questions, and we make steady progress with them.

Another handicap that we face more in physiological psychology than in any other part of psychology is that we usually cannot experiment on people. It is not safe to use many kinds of drugs and hormones with them, and it is not possible to remove various glands or parts of the nervous system at will. We therefore must do the best we can, not with human beings, but with animals. For that reason you will find the greater part of this book based on animals, not human beings. Fortunately, we know a good deal about evolution in behavior and in bodily form through the animals to man, and we frequently can make very good jumps from animal experiments to human beings, but we cannot always do it. We must simply recognize the limitation and make the best of it.

Scientific Inference. Experimental science is a complex process in which the "good" scientist indulges in a healthy mixture of experiments and hypotheses. From both his experiments and those of his comrades, he gets hunches, guesses, deductions, hypotheses, predictions—whatever one wants to call them—of what may happen under different circumstances, say, of another experiment. He then proceeds to test his hypothesis with an experiment. Sometimes he is right and sometimes wrong, but in any event his new experiment turns up ideas for more experiments, and he goes on around the cycle again. In the end it is the experiments that are important and the facts that we can trust—provided the experiments have been done right—and the hypotheses, crucial as they are to inspiring the scientist and leading him to the more important experiments, are simply the means to the end.

The cycle of experiments and hypotheses goes on in physiological psychology as it does in other sciences. Each experiment suggests tentative conclusions or hypotheses that lead to other experiments. This process will show up again and again in the book. We will stress the experimental facts, but we will try to show how one fact leads to the idea for the next experiment. In some places, too, where the experiments suggest an idea that has not been tested yet, we shall bring it out in the hope that you will see the way in which the next step may be taken—or perhaps you will do the experiment. This way of writing may sometimes include details of the scientific process that you do not really need to get the main points. Yet it keeps the facts and the theories straight, and it makes more vivid the steps investigators take in pushing our knowledge ahead and erasing our "ifs."

Not everyone makes a habit of going around the cycle of hypothesis and experiment. Some do experiments without any hypothesis in mind, and their experiments often do us very little good because they do not concern any question of interest. For that reason we shall say little or nothing about some experiments. We have some scientists who raise many interesting hypotheses but do very little experimenting. They call themselves theorists and have a place in the scheme of things. Where their ideas seem to be helpful, we shall explain them and use them. In general, however, we cannot spend too much time on theories or hypotheses that have not been put to the experimental test. There are many such notions—one could devote a whole book to them—but they can be, and often are, wrong. The facts, however, seldom lie, and we shall give them most of our space and attention.

The Meeting Ground of the Sciences. Perhaps no subject draws upon so many different sciences and their methods as does physiological psychology. Every sort of pure and applied scientist—mathematician, physicist, chemist, physiologist, pharmacologist, anatomist, neurologist, psychiatrist, electrical engineer, as well as psychologist—has been taking part in our subject in one way or another. None can claim sole or even major rights to the subject, for each has contributed a share. There is no point in taking up in detail what each of them has done and can do, but as you go along in the book you can see for yourself how the various sciences have met and joined hands to solve the problems of how events in the body link up with those of behavior.

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CHAPTER II

THE PERIPHERAL RESPONSE MECHANISM

The physiological machinery of behavior is exceedingly complex. In principle, however, it is simple. It consists of receptors, sensory nerves carrying messages inward from the receptors, a central nervous system made up of brain and spinal cord enclosed in the bony cases of the head and spinal column, motor nerves carrying impulses outward from the central nervous system, and finally the various effectors of the body such as muscles and glands. These are the essential parts involved in the adjustments of men and animals to their environments.

In this chapter and the next one we shall discuss these parts in some detail, in order that you will have a general background of knowledge of the structures involved in behavior. Later on, in chapters dealing with various aspects of behavior, additional details will be introduced as they are needed to deal with each particular problem. Here in these chapters we shall divide the summary into two parts: the peripheral response mechanism and the central nervous system. In this chapter we shall consider the receptors, the effectors, and the peripheral nerves going into and out of the nervous system.

THE FUNCTIONS OF CELLS

It was a discovery of great importance when Robert Hooke first observed (1665) that a very lowly organism, cork, is made up of cells. Subsequently many investigators observed cells in all kinds of tissues. Today we have come to recognize that the *cell doctrine* (1838) applies to all animals and plants. *The cell is the fundamental unit of living organisms.* We must therefore look to the cell first to see what kinds of building blocks are used in the machinery of behavior.

It is almost always possible to distinguish three principal and important parts of a cell: the membrane, the cytoplasm, and the nucleus. These three parts are interrelated. What happens in one part affects events in the other parts. Each part, however, has an important role to play in the life of the cell. Each part is primarily responsible for certain properties of the cell (see Fig. 1).

Properties of the Membrane. The membrane is the boundary of the cell. It will keep some things in, and some things out of, the cell. Because it is porous, however, it will allow many things to pass through. The "things" in this case are chemical molecules or charged ions making up the positive or negative parts of molecules. The study of the membrane therefore can, and does, become a matter of physical and biological chemistry. You will see that more clearly later when we take up some of the problems of membrane chemistry (Chap. V). Here, however, we can describe some of the properties of the membrane without delving too deeply into their chemical or physical explanations.

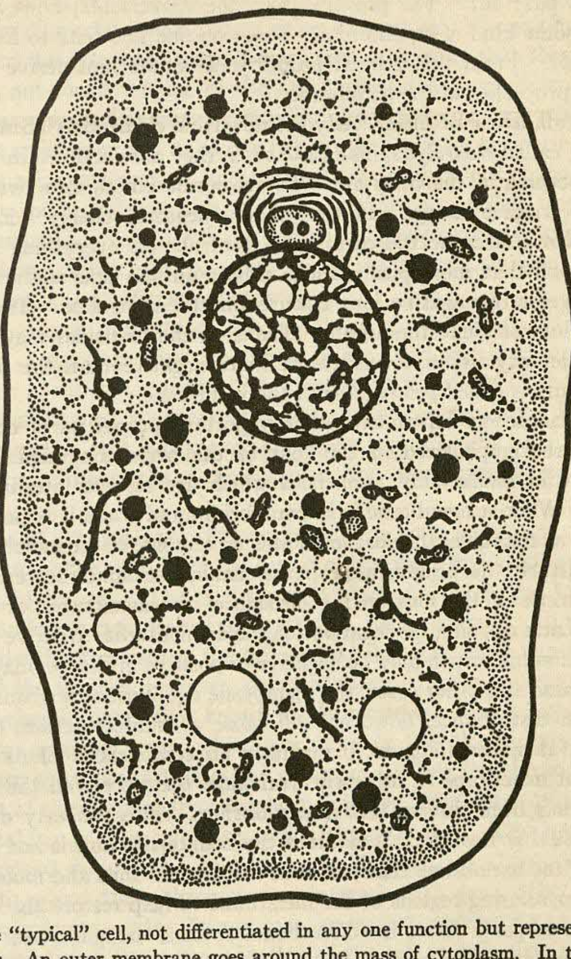

FIG. 1. The "typical" cell, not differentiated in any one function but representative of all kinds of cells. An outer membrane goes around the mass of cytoplasm. In the cytoplasm are many sorts of granules and a clearly marked nucleus which controls many of the activities of the cell. (*From R. W. Gerard. Unresting cells. New York: Harper, 1940. P. 77. By permission of the publishers.*)

One of the basic properties of the membrane is the maintenance of an equilibrium of pressures and of ions on the two sides of it. Some ions and molecules press from the outside inward; some from the inside outward. Some pass in and others pass out. The pressures and the movements, however, tend to remain in some kind of equilibrium. Those on one side tend to balance those on the other. From this general property of equilibrium derive some other important properties of the membrane.

Polarization is one of them. As you know from elementary chemistry, some substances, called *electrolytes*, dissociate when they are dissolved in water—and many substances in the body are. The molecule bursts into two parts, one carrying a positive charge and the other a negative charge. Each part is called an *ion*. Because the membrane does not let everything through, it often happens that more positive ions collect on one side of the membrane, while an excess of negative ions collects on the other side. There may be an equilibrium of ions—the number of ions on the two sides may be equal—but one side may be more positive or more negative than the other. This state of affairs is called *polarization* of the membrane.

From polarization derive two other important properties of cells that we shall later see emphasized in the cells of the nervous system. These are *irritability* and *conductivity*, properties which are always interlinked in cell functions. When a membrane is in equilibrium and when it is polarized, any loss of ions or change in the charges of ions on one side of the membrane breaks down or disturbs the equilibrium. A mechanical stimulus, for example, may knock off some of the ions on the outside of the membrane; or a chemical stimulus, made up, say, of negative ions, may neutralize positive ions; or an electrical stimulus, which may be negative or positive in charge, may neutralize ions. In these and other cases, the membrane equilibrium is disturbed.

Any such disturbance, however, will cause a counterreaction, because the membrane, as we said, tends to maintain an equilibrium. Ions may move through the membrane or otherwise rearrange themselves on the membrane, because it has been thrown into disequilibrium. This property of the membrane is called *irritability*. Sometimes the counterreaction is not confined to the part of the membrane that has been disturbed. Ions and molecules move about in neighboring regions of the membrane to help restore the equilibrium in the irritated part. Thus the disturbance spreads to regions nearby. These, in turn, cause disturbances in their vicinity. As a result, the disturbance runs along the whole membrane from one point to the next. When that happens, we speak of *conduction*—a very important property of certain cells in the body.

Properties of Cytoplasm. Cytoplasm is the main mass of the cell. It makes up the general area of the cell within the membrane and outside the nucleus. Cytoplasm varies enormously in its structure and chemical make-up. It usually has a great deal of water in it, and this in turn may have a number of chemical substances dissolved or suspended in it. Cytoplasm may contain many granules and minute structures, some of which are a great aid to the anatomist and physiologist who are trying to distinguish different kinds of cells and their state of health.

Generally speaking, however, there are two properties of the cytoplasm of cells that are of special interest to us. One is *secretion*. The various chemical substances in the cytoplasm may so react with each other that they make new substances, not found outside of the cell. These may remain in the cell to help with important functions in the life of the cell, or they may pass out through the membrane and be circulated to other cells for their use. The substances that are manufactured in the cytoplasm and pass out of the membrane to help out constructively with the life processes are called *secretions*. Of course, we must also recognize many substances made as waste products of the cell's chemistry, which also pass out of the membrane because the cell no longer "wants" them. These are *excretions*.

A second general property of the cytoplasm is *contractility*. This again is the product of some chemical reactions. When molecules change in shape or size or move about in a mass in such a way that the shape of the membrane and the cell is changed, we speak of contraction or contractility. It is through such changes that cells can move themselves about or, in highly developed organisms, move other cells of the organism and thus move the organism as a whole.

Properties of the Nucleus. The nucleus is the main body contained within the cytoplasm of the cell. It is the center of the most important activity that takes place in the cell. The nucleus certainly has a good deal to say about what goes on in the cytoplasm and, indirectly, the membrane. In many ways, it governs the life processes of the cell as a whole. The most important single property of the nucleus, however, is *reproduction*. In the nucleus are strands of complex chemical materials known as *chromosomes*. Making up part of the chromosomes are the genes, which are more or less the unitary characters which govern the reproduction of the organism. When the chromosomes split up, the rest of the nucleus, the cytoplasm, and the membrane usually split up too, each taking with it its share of the chromosomes. Two organisms are thus reproduced out of one. In sexual reproduction, two different cells must come together and their chromosomes interact with each other before the reproductive process starts. In any case, an important function of the nucleus and its chromosomes is the reproduction of the cell or cells that make up the organism.

In viewing the functions of the cell as a whole, we must note that the separation of properties of the membrane, cytoplasm, and nucleus is only a rough approximation. Actually the activities of all parts of the cell are closely interrelated and are involved, directly or indirectly, in its various properties. Depolarization of the membrane may, for example, cause the cytoplasm to contract or to secrete, and chemical conditions in the cytoplasm naturally affect the equilibrium and exchange of materials at the membrane. The present summary, however, brings out the important features of the cell in which we shall later be interested.

THE RESPONSE MECHANISM

We have been discussing a 'typical' cell, one that shows all the features of all the cells that we know in the human body. To a certain degree all cells in an organism possess all the properties that we have described. By the time we see them, however, in a grown animal or man, we see few, if any, cells that show all these properties in equal degree. Instead we find that various cells have become highly specialized in their functions. They have undergone what the cell physiologist would call *differentiation.* One type of cell is so differentiated in structure and function that it specializes in irritability and conduction —the nerve cell; another differentiates for irritability and contractility—the muscle cell; another for secretion—the gland cell; and so on. To get some appreciation of how this differentiation has taken place and what it has accomplished, let us look briefly at the scheme of cellular differentiation as we see it in the evolution of organisms and in their embryological development.

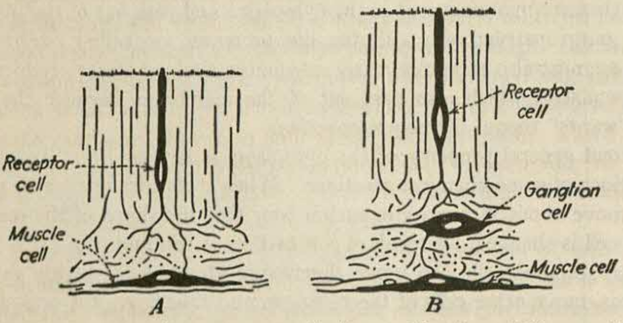

FIG. 2. Diagram of primitive response mechanisms. First in evolution was the muscle effector shown in *A*; the simple receptor-effector cell also in *A* was the next stage; and the third stage was the receptor-adjustor-effector mechanism of *B*. (*From G. H. Parker. The elementary nervous system. Philadelphia: Lippincott,* 1919. *Pp.* 201–202. *By permission of the publishers.*)

Differentiation. There are three classes of cells in which the physiological psychologist is most interested. These are the receptors, the nerve cells, and the effectors. Each class represents a high degree of specialization in one or more of the properties of cells which we took up a moment ago. These classes are not rigidly defined, for nerve cells often serve the functions of the receptors, but they will do for our purposes.

These three classes made their appearance very early in evolutionary history in very primitive multicellular organisms (see Fig. 2). As well as we can piece together this history, they developed in a particular order (Parker). The first to be differentiated was the muscle effector cell; it exhibits specialization of the properties of irritability and contractility. You can see an example of this first primitive effector in the common sponge. Later, the function of irritability was further specialized in a receptor cell—a cell whose principal function was to be excited by external stimuli and transmit the excitation to the effector. Such a receptor cell specialized in the property of irritability. Thus was differentiated a simple receptor-effector mechanism with which the organism could respond more effectively to its environment. Finally, we see developed the third class, eventually a tremendously important class, of cells. These are the adjustors, or more specifically the neurons, which became conductors between the receptors and effectors. They are called adjustors because they make possible a great variety of adjustive responses of the organism to the stimuli of its environment. They serve their purpose because they have greatly emphasized the property of conduction in their differentiation.

THE RECEPTORS

Having noted the primitive elements of the response mechanism—the receptors, effectors, and adjustors—we may go on to consider what happens to each of them in further evolution. All three types of cells are changed in many ways. But the receptors, perhaps more than any of the others, have developed more specialized forms that differ from each other in both structure and function.

Function. The first primitive receptors respond to all sorts of stimuli. Before long, however, receptors come to respond more to one type of stimulus than to another. In the end, four classes of receptors emerge: thermal receptors, mechanical receptors, chemical receptors, and photic receptors. As their names imply, they are specialized to respond most readily to different types of stimulus energy.

Despite specialization, however, receptors do not lose entirely their ability to respond to all types of energy. A photic receptor in the eye will respond to a thermal or a chemical stimulus if it is intense enough. Similarly a mechanical receptor can be excited by intense chemical stimuli. The specialization, therefore, is only relative, not absolute. And it is interesting too that all receptors retain their ability to respond to electrical stimuli. Such stimuli are not found often in nature, and there was no reason to develop a special sort of electrical receptor. But because of ionic polarization of the receptor membrane, all receptors are rather sensitive to electrical stimuli. This fact, as we shall see later, can be put to very good use in experiments with receptors.

Structure. Along with changes in the function of receptors also go changes in their form—although you cannot always tell the function of a receptor by looking at its structure. Structural differentiation of receptors proceeds in two general directions. One is the 'adoption' of an epithelial cell to make up part of a receptor structure. The other is the further differentiation of the neuron to perform a specific task. You can see examples of both types of structural differentiation in Fig. 3, which shows diagrams of three types of chemical receptors. One of them, the common chemical receptor, is the most primitive. It consists simply of a neuron with a free nerve ending. Another is the taste receptor, which consists of a neuron and a highly specialized epithelial cell that 'helps out' in the receptor's function. The third is an olfactory receptor, which is made up of a highly specialized neuron with special hairs on the end of it to make the receptor more sensitive to stimuli.

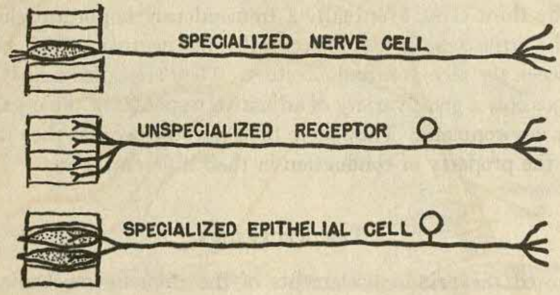

FIG. 3. Diagrams of three types of receptor cells. In the middle is the undifferentiated neuron with its epithelial cells. At the top is the receptor in which the neuron is highly differentiated, and at the bottom is the receptor in which the epithelial cells are differentiated. (*After Parker.*)

These are just examples of the directions in which receptor structure has gone. The structures serving other senses show a similar pattern in their differentiation. The visual receptors, like the olfactory, are simply highly specialized neurons. The mechanoreceptors as a class, however, follow the other line of differentiation. Those involved in simple pain are like the common chemical receptors; they are nerve cells ending freely among epithelial cells. The auditory and touch receptors, on the other hand, are characterized by the very special differentiation of the epithelial cells associated with them.

NEURONS

The nerve cell or neuron is the second of three links in the receptor-adjustor-effector mechanism. It has been differentiated for adjustment of activities between receptors and effectors. Of course, neurons sometimes participate in the differentiation of receptor mechanisms, as you have just seen, but the main duty of neurons is to make up the vast adjustor mechanism that we call the nervous system. To serve this purpose, the neuron has emphasized the properties of irritability and conductivity in its differentiation.

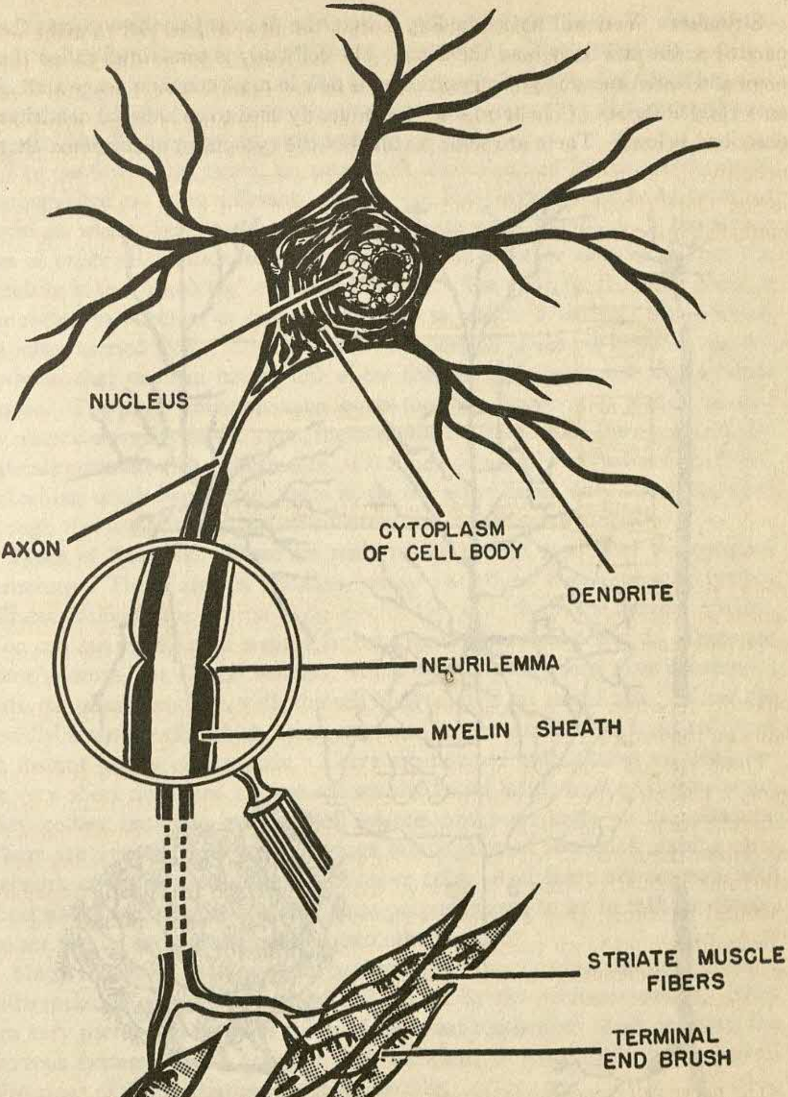

FIG. 4. A diagrammatic drawing of a neuron. At the top is the cell body and its numerous branchings, the dendrites. They make up the soma of the neuron. The axon, of which there is only one, extends downward. The point at which the axon leaves the soma is the axon hillock. Axons, and sometimes dendrites, may be covered with a myelin sheath and, outside the nervous system, a neurilemma.

Structure. You will notice in Fig. 4 that the neuron has three parts: the dendrites, the cell body, and the axon. The cell body is sometimes called the *soma* and sometimes the *perikaryon;* soma is now in most common usage among nerve physiologists. (The term soma is frequently used to include the dendrites described below.) There are some features of the cytoplasm of the soma that

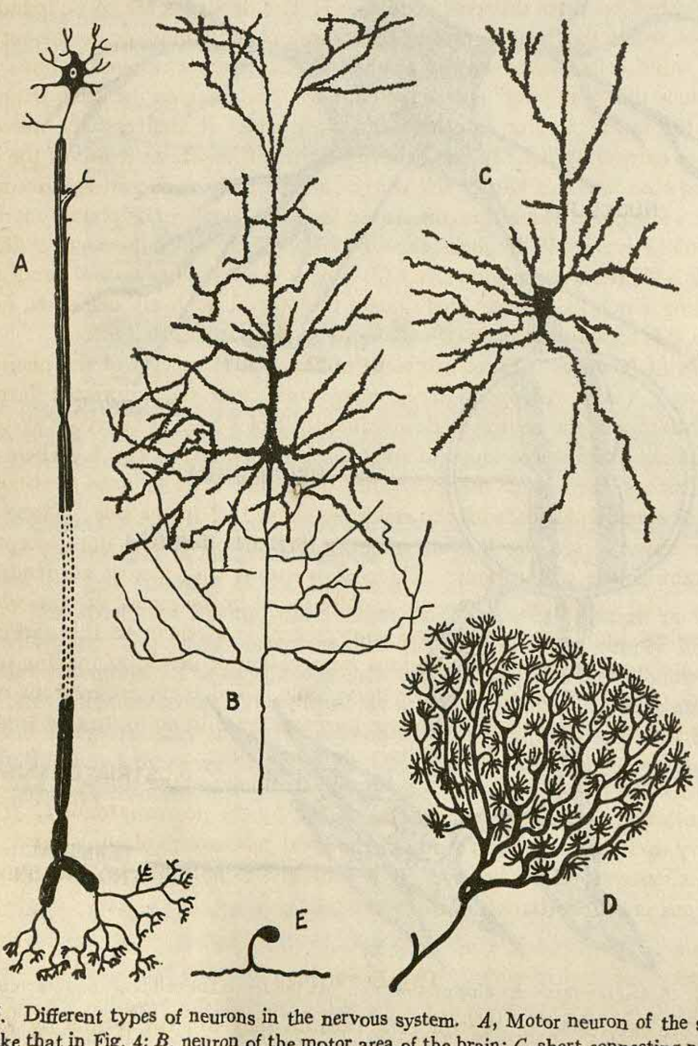

FIG. 5. Different types of neurons in the nervous system. *A,* Motor neuron of the spinal cord like that in Fig. 4; *B,* neuron of the motor area of the brain; *C,* short connecting neuron called *Golgi type II; D,* a bushy cell found in networks of neurons; *E,* bipolar neuron of sensory nerves. *(From C. L. Evans. Starling's principles of human physiology. 9th ed. Philadelphia: Lea & Febiger,* 1945. *P.* 192. *By permission of J. & A. Churchill Ltd.)*

have become rather specialized and are of some use in the study of the nervous system, but we shall pass them by for the present. Most conspicuous in the differentiation of the nerve cell are the two kinds of fibers, the dendrites and the axon. These, as you can see, emphasize the properties of the membrane of cells, *viz.*, irritability and conductivity.

The dendrites and axons, in turn, have their separate features and can be distinguished on three different counts. (1) The dendrites are to be found in positions where they can be excited by environmental stimuli or by the activities of other cells, either sensory epithelial cells or other neurons. Thus the dendrite is the "receiving" end of the neuron. The axon, on the other hand, is connected to effectors or to other neurons to which it 'delivers' the nervous impulses carried by it. (2) The dendrite tapers off in size as it leaves the cell body so that one can hardly tell where the cell body ends and the dendrite begins. The place where the axon leaves the soma, however, is plainly marked by a small elevation in the soma, the *axon hillock*, from which the nerve cylinder extends outward with uniform size. (3) A neuron usually has several dendrites, branching much like a tree; there is, on the other hand, only one axon, even though this sometimes sends off collaterals at right angles to itself.

Types of Neurons. Those are some of the typical aspects of the neuron's structure. There are, in addition, many variations that represent further differentiation of the neuron to do specific types of jobs in the nervous system. You can see examples of some different kinds of neurons in Fig. 5. There are some neurons, the *bipolar neurons*, which have one very long axon continuous with one short dendrite, with the cell body shoved off to the side. These are usually sensory cells which bring messages to the spinal cord from receptors at distant points of the body. There are neurons with almost no dendrites or very short dendrites. These are usually found in the motor system, where they collect impulses from several sources and send them to the effectors. There are neurons with a tremendous ramification of dendrites making up a network of endings on many other nerve cells. And there are neurons with short axons and short dendrites whose purpose seems to be to make a simple, rather precise connection between two other neurons.

Many classes and subclasses of neurons, according to their different kinds of differentiation, have been defined and named by the neuroanatomists. They are very useful in a detailed study of the great mechanism of adjustment, the nervous system. Here, however, it is sufficient to note briefly these general directions of differentiation of the nerve cells.

THE EFFECTORS

We are interested in effector cells because they are the means by which the organism responds to the world. Effector cells, like the other kinds of cells, have differentiated in both structure and function. In vertebrate animals there are two main classes of effectors, the muscles and the glands.

Muscles. These are divided into different types. In Fig. 6 you can see examples of three main kinds of muscle. One, the most primitive and least differentiated, is the nonstriated or *smooth* muscle cell. In the typical case it is spindle-shaped. It contains within it strands of a special substance, the fibrillae, whose change in shape is what makes the muscle contract. *Striated* muscles, a second class, are more elaborate in form. They are much more elongated than are smooth muscle cells, and they are enclosed in a special elastic membrane, the sarcolemma. Within this membrane are the fibrillae that contract, and these are differentiated into two substances, one darker than the other. Because the fibrillae are regularly alternated throughout the muscle cell, they give the muscle a striped or striated appearance under the microscope. Finally there is a third kind of muscle, *cardiac* muscle, that is really just a special kind of striated muscle. Its chief distinction is that its fibers are not arranged in parallel as are the striated muscle cells, nor are they enclosed in a membrane, but they branch and unite in a network, or syncytium.

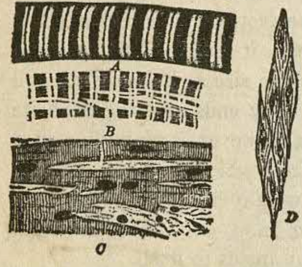

FIG. 6. Types of muscle cells. *A* and *B* are striped muscle fibers, *C* shows the muscle fibers of the heart, and *D* is a sketch of some smooth muscle fibers. (*From M. F. Guyer. Animal biology. 3d ed. New York: Harper*, 1941. *P.* 405. *By permission of the publishers.*)

Glands. In most instances glands receive effector neurons from the nervous system, and they therefore rate as a class of effectors. Their function usually is to secrete chemical substances that are important to the life of the organism. Thus glands make adjustments of the internal environment just as muscle effectors make adjustment in and to the external environment.

There are many different glands, and we shall consider some of them later. Here we should recognize two major classes of glands, the duct and the ductless. The *duct* glands empty their secretions into the cavities of the body, *e.g.*, the duct glands of the digestive tract, whereas the ductless glands put their secretions directly into the blood. Because they are circulated in the blood, secretions of ductless glands have a more profound effect on the body as a whole and on nervous activity in particular. We therefore shall later become most interested in them.

THE PERIPHERAL NERVOUS SYSTEM

You now have a general idea of the cells that make up the response mechanism and of their properties. Later on, when we take up each of the senses in turn, there will be a detailed description of the anatomy and physiology of each of the receptor organs of the body. Similarly, when we come to motor functions, there will be more discussion of the effectors, how they are constructed, and how they work. For the present, therefore, we need not spend any more time on the receptors and effectors. The peripheral nervous system, however, being so elaborate and being involved in all of the receptors and effectors, needs some further description.

Definition of Terms. To present even the most general aspects of neuroanatomy is no simple matter. We certainly need every aid to understanding that we can grasp. One of these is a system of terminology that has been developed for dealing with the central and peripheral nervous system. The terminology uses the brain and spinal cord as its point of reference, but it is necessary and useful in dealing with the peripheral nervous system as well. It is illustrated in Fig. 7.

The terms *anterior* and *posterior*, better limited to the brain only, refer to the front and back of the head, respectively. *Rostral* and *caudal*, on the other hand, we shall restrict to the spinal cord, where they will mean headward and tailward, respectively. *Dorsal* refers to the top of the head or to the back of the spinal cord, whereas *ventral* is used to indicate the bottom of the brain and the side of the spinal cord nearest the abdominal cavity. *Medial* is in the direction of the mid-line of the body, and *lateral*, away from it. Finally, we use *proximal* and *distal* to indicate what is near to and far from some given position, respectively. All these terms indicate direction or relative position and do not in any way refer to a specific locus.

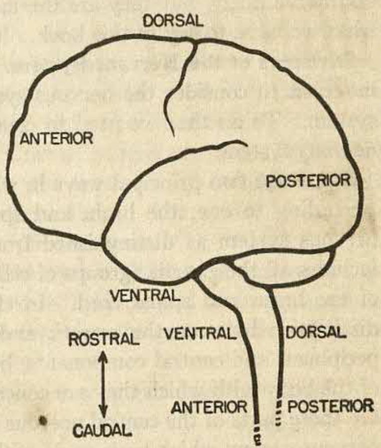

Fig. 7. Side view of the human brain illustrating the various terms used in neurology to denote direction or position.

Gray Matter and White Matter. There is another general feature of the nervous system that is convenient to know and use—its color. Neurons are naturally gray in appearance. Many nerve fibers, however, have a cover on them, the *myelin sheath*, which is white. Whenever a part of the nervous system looks white we know immediately that it is made up, in whole or in part, of myelinated fibers. The cell bodies of neurons, on the other hand, are never covered with myelin, and they consequently are always gray. So when we see gray matter in the nervous system we know it consists of cell bodies. Gray matter and white matter, therefore, are convenient terms for distinguishing the clumps of cell bodies from tracts or nerves made up of fibers.

Centers and Pathways. There are other terms that will be used a lot in the pages that lie ahead. These, too, have to do with cell bodies and fibers. Fortunately for the student, the nervous system frequently has cell bodies and

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nerve fibers in separate places. A clump of cell bodies is called either a *ganglion* or a *nucleus*. In general, when the clump is outside the brain or spinal cord it gets the name ganglion, and usually but not always a clump within the central nervous system is called a nucleus. On the other hand, nerve fibers when gathered together in a bundle may be called *nerves* or *tracts*. The term nerve is used for such bundles outside the central nervous system, and the term tract refers to such bundles within the brain or spinal cord. These terms—ganglia, nuclei, tracts, and nerves—are not the only ones used for clumps of cell bodies and nerve fibers, but they are the most common ones and will do for most of what we have to say in this book.

Divisions of the Nervous System. Now, with these terms in mind we can move on to consider the nervous system, particularly the peripheral nervous system. To do that we need to consider first the general organization of the nervous system.

There are two principal ways in which the nervous system may be divided. According to one, the brain and spinal cord together constitute the *central* nervous system as distinguished from the *peripheral* nervous system, which includes all the ganglia (groups of cell bodies) and nerves (nerve fibers) outside of the brain and spinal cord. In classifying them in another way we may distinguish between the *somatic* and *autonomic* nervous systems. Each has peripheral and central components, but their distinguishing feature is the part of the body with which they are concerned. Included in the autonomic system are those parts of the central nervous system and those nerves of the peripheral nervous system which have to do with the responses of (1) the smooth muscles of the intestines, urogenital tract, and blood vessels; (2) the muscles of the heart; and (3) those endocrine glands which receive a nervous supply. In general, the autonomic system controls the internal environment. In the somatic nervous system is included all those parts of the central and peripheral nervous system that convey impulses from the sense organs, organize them in the brain, and deliver motor impulses to the striated skeletal musculature of the body and limbs.

Although the peripheral endings of the autonomic and somatic nervous systems are quite distinct, there is no clear separation of them in the central nervous system or even in the main trunks of peripheral nerves. In the latter, we can sort out to some extent the autonomic and somatic fibers on the basis of known differences in fiber types and by tracing the fibers to their terminations. Some centers of the central nervous system, on the other hand, are concerned principally either with autonomic functions or with somatic activities. But such divisions of function are always a matter of degree, and autonomic and somatic processes are always closely coordinated. That is to be expected, because adjustments of the internal environment of the nervous system are always essential to somatic adjustments, and vice versa, and the two mechanisms therefore must be thoroughly interlinked.

So much for the general features of the nervous systems. Now let us consider some of the details. The rest of this chapter deals with the peripheral nervous system, first the peripheral somatic system and after that the peripheral autonomic system.

THE PERIPHERAL SOMATIC SYSTEM

This system is made up of nerves and ganglia. It is usually considered in two parts, cranial and spinal, depending on the part of the central nervous system from which the nerves and ganglia take origin. Motor fibers of both cranial and spinal nerves have their cell bodies within the central nervous system, usually in the ventral region nearest the point of exit of the fibers. Sensory fibers, on the other hand, always have their cell bodies in ganglia outside of the central nervous system. Cranial ganglia are to be found here and there in the recesses of the skull near the several small holes in the skull that serve as entrances and exits for nerve fibers. The spinal ganglia are arranged much more regularly along the spinal column.

The Cranial Nerves. One ordinarily distinguishes 12 sets of cranial nerves. Their names and functions are summarized in Table 1, and their arrangement is illustrated in Fig. 8. The first two nerves, the olfactory and the optic, are

TABLE 1. THE NAMES, FUNCTIONS, AND ORIGINS OF THE CRANIAL NERVES

Number	Name	Functions	Origin or end in the brain
I	Olfactory	(s) Smell	Cerebral hemispheres (ventral part)
II	Optic	(s) Vision	Thalamus
III	Oculomotor	(m) Eye movement	Midbrain
IV	Trochlear	(m) Eye movement	Midbrain
V	Trigeminal	(m) Masticatory movements	Midbrain and pons
		(s) Sensitivity of face and tongue	Medulla
VI	Abducens	(m) Eye movement	Medulla
VII	Facial	(m) Facial movement	Medulla
VIII	Auditory vestibular	(s) Hearing (s) Balance	Medulla
IX	Glossopharyngeal	(s) (m) Tongue and pharynx	Medulla
X	Vagus	(s) (m) Heart, blood vessels, viscera	Medulla
XI	Spinal accessory	(m) Neck muscles and viscera	Medulla
XII	Hypoglossal	(m) Tongue muscles	Medulla

purely sensory in function. Neither of them is a true nerve, however, in the sense that nerves ordinarily consist only of fibers pushed out from the nervous system. Instead these nerves represent portions of brain tissue which have migrated from the central nervous system to form the retina of the eye and the olfactory membrane but which, nevertheless, have maintained their connections with the brain. Three other nerves, the IIIrd, IVth, and VIth, are made up entirely of motor fibers innervating the muscles of the eye and concerned with its movement. The central nuclei of these nerves make up an important center for the control of eye movements, later to be taken up in detail.

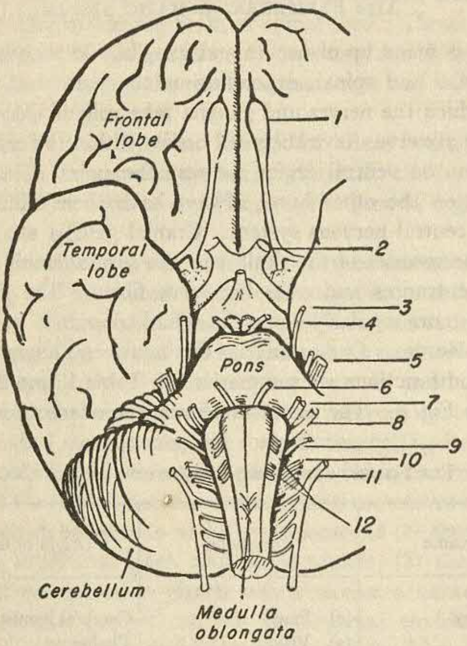

FIG. 8. A ventral view (looking from underneath) of the brain showing the cranial nerves. Each number is the number of a nerve. In Table 1 you can see the name that goes with each number and the function of the various nerves. (*From C. H. Best and N. B. Taylor. The living body. 2d ed. New York: Holt, 1944. P. 451. By permission of the publishers.*)

The Vth cranial nerve, the *trigeminal*, is the nerve most important for sensations and movements of the mouth. It carries tactile sensations from the face, tongue, and mouth, and it is the principal motor nerve concerned with chewing. Its motor functions in chewing, tongue movement, and swallowing are augmented, however, with the services of two other nerves, the *glossopharyngeal* (IXth) and *hypoglossal* (XIIth). Then, too, in the trigeminal's control of facial movements the facial (VIIth) nerve takes a part. Certain of these nerves are also involved in taste reception. Of these the most important is the facial (VIIth), which serves about two-thirds of the tongue, but the glossopharyngeal (IXth) and the *vagus* (Xth) also help out by innervating the taste buds of the back part of the tongue and throat. This vagus nerve is mentioned here only in passing, but we shall see later on that it is quite important in autonomic functions. To make the list complete let us note that the VIIIth nerve is a purely sensory nerve carrying auditory and vestibular impulses from the internal ear.

The Spinal Somatic Nerves. These are more regularly arranged and more uniform in their function than the cranial nerves. There are 31 pairs of them (in man) disposed at regular intervals along the spinal cord. They enter and leave the cord through spaces between the spinal vertebrae. They may be classified into five groups, according to the part of the cord with which they are associated (see Table 2).

TABLE 2. THE NAME, NUMBER, AND POSITION OF THE SPINAL NERVES IN MAN

Name	Number	Position
Cervical.....	8	Neck
Thoracic.....	12	Chest
Lumbar.....	5	Loin*
Sacral.......	5	End of spinal column
Coccygeal....	1	End of spinal column

An important aspect of the spinal nerves is the *law of roots*. You can see it illustrated in Fig. 9. Just before entering the vertebral column the spinal nerves divide into two roots. Of these, the dorsal root is sensory in function and the ventral root motor (although there are exceptions). On each dorsal root there is a marked swelling, the *dorsal* spinal *ganglion*, that contains the cell bodies of the sensory fibers passing through it from the sense organs into the spinal cord. It is within the spinal cord itself, however, that the cell bodies of the motor fibers are to be found. Because these cell bodies form a mass of gray matter in the ventral part of the cord resembling a horn, they are frequently spoken of as the *ventral horn cells*.

The sensory portions of the spinal nerves come from the tactual, thermal, and pain receptors of the skin; from the receptors in the blood vessels; from pressure and pain receptors in the muscles, tendons, and joints; and to some extent from the internal receptors in the digestive tract and body cavities. As this list plainly indicates, the sensory roots of the nerves mediate sensitivity of most of the body except the face. Similarly, although each nerve has its distribution confined to a relatively small area of the body (dermatome, see page 260), the motor portions of the spinal nerves control all the striated muscles of the arms, legs, and body except for those of the head and neck.

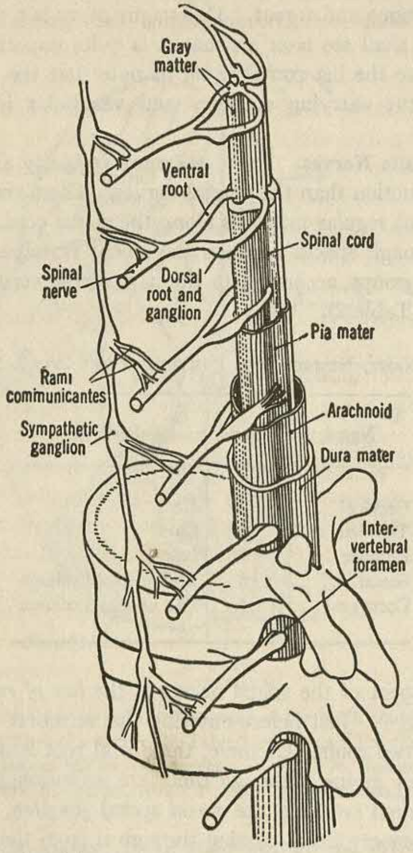

FIG. 9. A three-dimensional diagram of the spinal cord, the spinal nerves, and the bony case of the spinal cord. Two vertebrae are in the lower part of the drawing, and seven segments of spinal nerves are shown. Notice the ventral and dorsal roots of the cord, also the dorsal ganglion, an enlargement on the dorsal root. The arachnoid, dura mater, and pia mater are the three meninges (coverings) of the nervous system. Spinal nerves connect with sympathetic ganglia of the autonomic system through the *rami communicantes.* See page 29 of the text for further explanation. (*From E. Gardner. Fundamentals of neurology. Philadelphia: Saunders,* 1947. *P.* 34. *By permission of the publishers.*)

THE PERIPHERAL AUTONOMIC SYSTEM

As we have already said, the autonomic system is concerned principally with internal adjustments of the organism, whereas the somatic system has to do with adjustments between the external world and the organism. Correlated with the different roles played by these two systems are certain differences in their structure and activities. (1) The somatic system embraces both sensory and motor activities, but the autonomic is considered only as a motor system. There are, however, sensory fibers innervating the viscera that are plainly concerned with autonomic motor functions. (2) All the synapses of the somatic system, except for the special cases of the retina and olfactory bulb, are to be found within the central nervous system; on the other hand, it is signally characteristic of the autonomic system that many of its synapses and its ganglia lie outside the central nervous system. (3) In respect to organization of functions, the two systems differ in that the autonomic tends to function more as a whole and is less differentiated than the somatic system. (4) They differ also in distribution of fibers, for, as we have already seen, the autonomic system innervates the glands and smooth muscles of the viscera and blood vessels, whereas the motor somatic system is distributed to the striated muscles of the periphery.

Divisions of the Autonomic System. We distinguish two channels of outflow of nervous activity in the autonomic nervous system (see Fig. 10): (1) the *orthosympathetic* (commonly known simply as the *sympathetic*) outflow takes place through the *thoracic* and *lumbar* regions of the spinal cord, and for this reason it is sometimes referred to as the thoracicolumbar system; (2) the *parasympathetic* division takes its origin in the *cranial* and *sacral* regions of the central nervous system, and it may accordingly be called the *craniosacral system.*

The two divisions are largely, although not completely, antagonistic in their effects. In general, the sympathetic system *mobilizes* the resources of the body for use in work and special emergencies, while the parasympathetic system *conserves* and stores bodily resources. In other words, the first helps *spend* bodily resources (catabolism) and the second helps *save* them (anabolism). This statement, although true in general, does not hold in certain specific instances. Naturally, too, these two systems never act independently of each other but are brought into correlated activity in varying degrees, depending upon the demands made on the organism by the external world. Through their antagonistic yet coordinated action, a comparatively stable equilibrium of the internal environment is maintained under many different conditions of work and rest. How that is done will be illustrated in the more detailed treatment of the two systems that follows.

The Orthosympathetic System. Spinal paths of conduction exist for the autonomic system just as in the somatic motor system. The motor cells of the autonomic system tend, however, to be found in the lateral parts of the spinal gray matter rather than in the ventral horns as are the somatic motor neurons. In the thoracicolumbar segments of the spinal cord, the axons of autonomic cells pass out the ventral roots with the somatic motor axons and make up part of the ventral roots. Just outside the spinal cord, however, these sympathetic axons leave the main nerve root and enter a *sympathetic ganglion*, where they end upon the cell bodies of other neurons.

Structure. There are 22 sympathetic ganglia (in man), arranged regularly along the spinal cord and constituting the so-called "sympathetic chain," or ganglionic cord. In the ganglia of this cord end the fibers originating in the spinal cord as just described. These fibers we call *preganglionic* fibers. Because

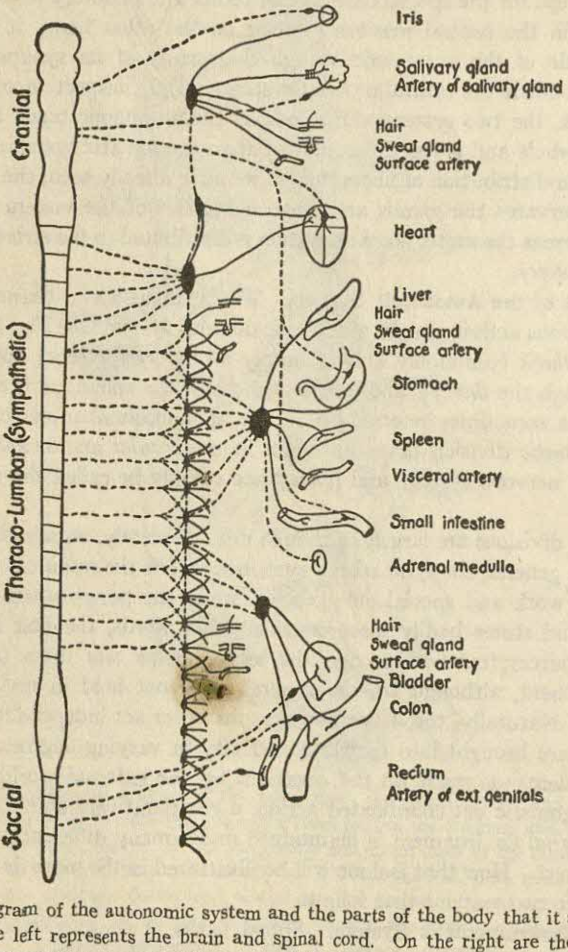

FIG. 10. Diagram of the autonomic system and the parts of the body that it serves. The column on the left represents the brain and spinal cord. On the right are the autonomic ganglia, the autonomic nerves, and the organs of the body to which they go. The diagram represents only the right side of the body, not the left. The dashed lines from the central nervous system to the autonomic ganglia are preganglionic fibers; those from the ganglia to the peripheral organs are postganglionic fibers. (*From W. B. Cannon. Bodily changes in pain, hunger, fear and rage. 2d ed. New York: Appleton-Century-Crofts,* 1929. *P.* 23. *By permission of the publishers.*)

they are mostly myelinated, the branch that they make up after leaving the spinal nerve is called the *white ramus*. The cell bodies in the ganglion send axonal fibers back to the spinal nerves as shown in Fig. 11, and because these are unmyelinated they are known as the *gray ramus*. Fibers in this ramus we call *postganglionic* fibers.

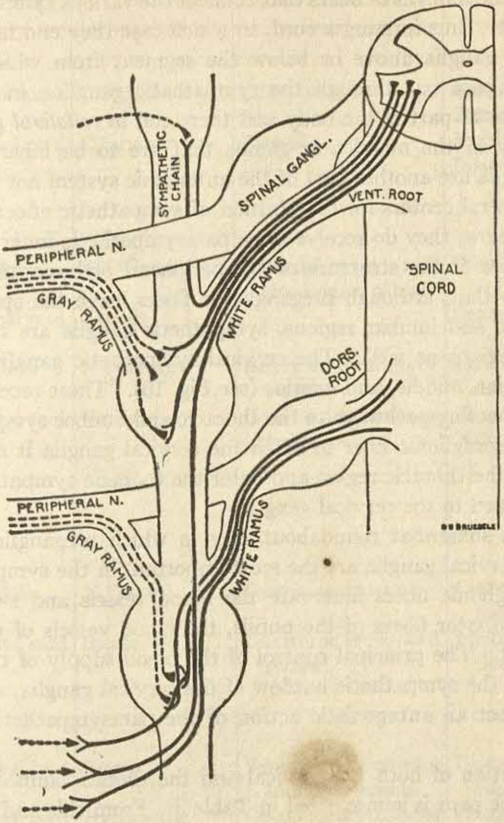

FIG. 11. Diagram of the relations of autonomic ganglia, spinal cord, and peripheral nerves in the sympathetic system (thoracicolumbar outflow). Preganglionic fibers, making up the white rami, leave the lateral columns of the spinal cord and proceed by way of the ventral nerve roots to the sympathetic chain, where they terminate at various levels. The postganglionic fibers, making up the gray rami, join the peripheral nerves or blood vessels and thence are distributed to the peripheral organs, which they innervate. (*After Edinger. From J. F. Fulton. Physiology of the nervous system. New York: Oxford,* 1938. *P.* 208. *By permission of the publishers.*)

Not all the fibers leaving the sympathetic ganglion go back to the spinal nerve, nor do all the preganglionic fibers from the spinal cord end in the nearest ganglion of the sympathetic cord. As shown in Fig. 11, they may pursue any one of three courses: (1) they may end upon the cell bodies in the nearest sympathetic ganglion as described above; (2) they may pass through that ganglion into the bundles of fibers that connect the various sympathetic ganglia with each other, thus forming a cord, in which case they end finally upon the cell bodies of ganglia above or below the segment from which they came; (3) they may pass out through the sympathetic ganglion in an autonomic nerve to the distal part of the body and there end in *collateral ganglia* located in the vicinity of the muscles or glands that are to be innervated. These collateral ganglia are another part of the autonomic system not yet mentioned and are peripheral centers for distribution of sympathetic effects although, as we shall see below, they do receive some parasympathetic innervation.

A final aspect of the structure of the peripheral orthosympathetic system to be noted is that, although preganglionic fibers leave the spinal cord only in the thoracic and lumbar regions, sympathetic ganglia are to be found in the cervical regions as well. The cervical sympathetic ganglia are three in number: superior, middle, and inferior (see Fig. 10). These receive their fibers by way of connecting pathways to the thoracic and lumbar sympathetic chain. Thus for a preganglionic fiber to reach the cervical ganglia it must leave the spinal cord in the thoracic region and enter the thoracic sympathetic cord and then turn upward to the cervical ganglia.

Despite this somewhat roundabout way in which preganglionic fibers get to them, the cervical ganglia are the most important in the sympathetic chain. Their postganglionic fibers innervate the blood vessels and sweat glands of the head, the dilator fibers of the pupils, the blood vessels of the heart, and the heart itself. The principal control of the blood supply of the brain is, in fact, vested in the sympathetic outflow of the cervical ganglia, although there is in this respect an antagonistic action of the parasympathetic system (see below).

The distribution of both the cervical and the thoracicolumbar divisions of the sympathetic cord is summarized in Table 3. From this and Fig. 10 it can be seen that the thoracicolumbar chain innervates all the other organs of the viscera below the heart: the liver, stomach, intestines, bladder, urogenital organs, and adrenal glands. In the vicinity of these organs are three ganglia bearing the names of, and distributed to, the organs indicated in the figure.

Function. Turning now to the more functional aspects of the sympathetic system, we may refer again to the general fact that the sympathetic system mobilizes rather diffusely the resources of the organism. Because this is of particular importance when the organism is threatened with danger and has strenuous work to do, the sympathetic system has been thought of as subserving *emergency* functions. In the light of this generalization, the significance of the principal effects of sympathetic activity becomes clear: widening of the pupils, constriction of visceral blood vessels so that blood is directed to the

TABLE 3. AUTONOMIC PATHWAYS AND THEIR FUNCTIONS

Organ	Origin	Nerve	Effector	Function
Eye:				
Para....	Midbrain	III (Oculomotor)	Ciliary muscle Iris	Accommodation Contraction
Ortho...	Spinal cord	Ciliary nerve	Eyeball Iris	Exophthalmos Dilation
Cerebral arteries:				
Para....	Medulla	VII (Facial)	Carotid artery and blood vessels of brain	Dilation
Ortho...	Spinal cord	Various		Contraction
Heart:				
Para....	Medulla	X (Vagus)	Heart and coronary vessels	Inhibition and coronary constriction
Ortho...	Spinal cord	Various	Heart and coronary vessels	Acceleration and dilation
Stomach and small intestine:				
Para....	Medulla	X (Vagus)	Gastric musculature	Contraction and secretion
Ortho...	Spinal cord	Splanchnic	Gastric muscles and glands	Inhibition of contraction and secretion
Genitourinary tract:				
Para....	Spinal cord	Sacral	Genitourinary muscles and blood vessels	Urination, defecation, vasodilation, erection
Ortho...	Spinal cord	Hypogastric	Genitourinary muscles and blood vessels	Contraction of sphincters, prostate, and seminal vesicles, inhibition of rectum and bladder
Arteries of body:				
Para....	Spinal cord	Various	Blood vessels	Dilation
Ortho...	Spinal cord	Various	Blood vessels	Contraction

muscles and brain, acceleration of the rate of heartbeat, inhibition of intestinal and gastric activity, secretion of adrenalin with the result that blood sugar is raised and tissue metabolism increased—all these effects prepare the organism to deal with an emergency situation. Further details concerning the sympathetic system and its functions may be found in Table 3.

The Parasympathetic System. As we have already seen, the sympathetic system has ganglia either in the region of the spinal cord or in the vicinity of the organs that it innervates. Only in the latter situation, however, do we find the ganglia of the parasympathetic division. This has long preganglionic fibers arising either in the brain or in the sacral division of the spinal cord and extending to the parasympathetic ganglia, which are always close by the tissues to which their fibers are distributed. Thus there is no chain of parasympathetic ganglia by which nervous effects can be interrelated. From such a structural difference in the two systems one may surmise a characteristic functional difference, *viz.*, that the sympathetic division tends to act more diffusely and as a whole, whereas the parasympathetic division is a more highly differentiated system which is more capable of independent activity in each of its parts.

Because the parasympathetic division is fairly specific in its various functions, neurologists have been able to distinguish several subdivisions which have their respective duties. It will do us no good, however, to go into such details. Only two general subdivisions are worth noting. These are the cranial and sacral parts of the parasympathetic division. The cranial part consists of all the nerves and outlets which are associated with the brain and the head. This part serves, among other things, the iris of the eye, the salivary glands, and the heart. The sacral part comes from the extreme lower end of the spinal cord. It serves the bladder, the colon, the rectum, and the arteries of the genitals.

The general functions of the parasympathetic system are those of the conservation of bodily resources and the building up of the body. Thus the parasympathetic outflow causes constriction of the pupil, a response that serves to protect the eye from excessive light. It inhibits the heartbeat and causes vasodilation, in this way lowering blood pressure, which reduces the utilization of fuels throughout the body. It participates in digestion, definitely a constructive process, in several ways: by increasing the rate and amount of salivary secretion, by increasing contractions of the stomach, by causing digestive juices to be secreted into the stomach. Through the sacral outflow, moreover, the parasympathetic division frees the body of unwanted, and perhaps even poisonous, materials by causing emptying of the bladder and colon.

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CHAPTER III

THE CENTRAL NERVOUS SYSTEM

As we noted before, the central nervous system is the organ that is housed in the bony case of the skull and the spinal column. It can be subdivided and named in various ways. The big division, which is easy to see, is into brain and spinal cord. The brain, however, is further divided into five main parts: the telencephalon, the diencephalon, the mesencephalon, the metencephalon, and the myelencephalon. These are big words, which are undoubtedly unfamiliar to the beginning student in physiological psychology. They happen, however, to be the best classification for us to use in dealing with the central nervous system. In this chapter, therefore, we shall consider the central nervous system under six heads, the spinal cord and the five divisions of the brain just named. It will become clear as we go along what these names refer to.

METHODS OF STUDYING THE NERVOUS SYSTEM

Before we get into the detailed anatomy of the central nervous system, it is well to consider some of the methods which neuroanatomists and neurophysiologists use in studying its structure and function. Different methods tell us different things about the nervous system, and by combining different methods we learn things not given by any individual method by itself. Moreover, new methods are coming into use each year, and as they do, modern neurological research continues to tell us new and important facts about the structure of the nervous system.

Descriptive Methods. The oldest of the methods of studying the nervous system is the simple description of what one sees when one looks at the nervous system with the naked eye or in cross section under the microscope. To see things more clearly the investigator ordinarily uses one or more of a variety of methods of staining the nervous system. In general, there are two kinds of staining methods that can be used. One stains the soma of the neuron, including the granules and other special features of the cytoplasm and nucleus of the cell. The other leaves the soma of the neuron relatively untouched but stains the fibers of neurons and their sheaths. Fibers themselves, however, are rather hard to stain, although there are methods for doing it that are sometimes used. Much easier and much more often used is a method for staining the myelin sheath of the fibers. In this way it is relatively easy to trace the fibers of neurons around the nervous system. The only difficulty with such a myelin-staining method is that many fibers of the nervous system are not myelinated or are so thinly myelinated that they cannot be seen with a myelin stain.

When the neurologist uses these staining methods on the neurons of the central nervous system and describes what he sees, he usually finds that cell bodies of neurons are gathered in small clumps called *nuclei*. He can locate the various nuclei and give them names. With fiber- or myelin-staining methods he can also see large numbers of fibers gathered together, making up a *tract*, or *fasciculus*, that he can trace throughout its length in the nervous system. By seeing what nuclei various tracts come from and go to, he can get a fair idea of how the nervous system is put together.

Degeneration Methods. The simple descriptive methods have their limitations. Because unmyelinated fibers do not stain very well and because the connections in the nervous system are so microscopically small, there are many connections and relations between fibers and somas that completely escape this method of study. Another method which supplements the simple descriptive method is the degeneration method. In order to use it, it is necessary to know something about the conditions under which various fibers and cell bodies undergo degeneration in the nervous system.

The term *degeneration* applies to a variety of changes in neurons indicating ill health and possible death of the neuron. One important sign of partial or total degeneration of the neuron is the disintegration and disappearance of the substances of the soma and dendrites. In Fig. 12 you see, for example, two different materials in the cytoplasm of the neuron that undergo change or disappearance when the cell is fatigued, dying, or dead (see Fulton). The first series of changes (*A*) is in the Golgi apparatus, which first moves to the periphery of the soma, then fragments, and eventually disappears as the neuron dies. The second set of diagrams shows the *Nissl granules*, or *chromidial substance*—either name will do—at different stages in the dying cell. This sign is the one used most frequently in research studies, and the changes are spoken of as *chromatolysis*.

In addition to these signs of degeneration, there are three types and conditions of degeneration which we should note. (1) If fibers are severed from their cell bodies, the part of the fiber distal to the place of the cut will degenerate and die. This is *Wallerian degeneration*, and it occurs in all neurons. In fibers outside the central nervous system, however, the part of the fiber still attached to the cell body ordinarily will begin to grow and will eventually replace the part that has degenerated. (2) In the brain and spinal cord, on the other hand, such regeneration usually does not take place. Instead, not only does the distal fiber degenerate, but the proximal fiber and indeed the whole neuron dies. This kind of degeneration has been called *secondary degeneration*. It is used as a standard method by neurologists in tracing connections and nuclei in the central nervous system. When, for example, fibers have been cut in one part of the nervous system and a nucleus is found somewhere else with many of its cell bodies partially or totally degenerated, we can be rather sure that the cell bodies are the ones that belong to the fibers that were cut. (3) Still a third type of degeneration, *transneural degeneration*, occurs only rarely and then only in certain parts of the central nervous system. In this case, because other cells have died and left them without their normal connections, cells may undergo chromatolysis and death without themselves having incurred any direct injury.

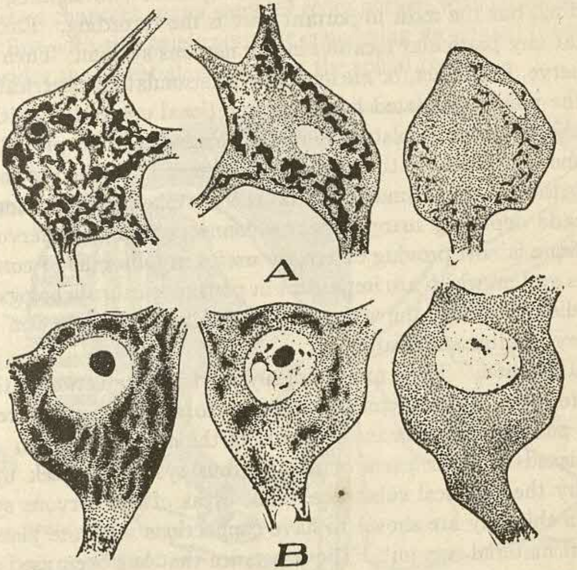

FIG. 12. The principal structures in a neuron of the spinal cord and the changes they undergo when they are injured. *A*, Golgi apparatus: left, normal cell; middle, partial loss and migration to periphery one week after sectioning the axon of the neuron; right, almost complete disappearance of Golgi apparatus after cutting of the spinal cord. (*After Penfield*, 1920.) *B*, Nissl substance: left, a normal cell; middle, moderate chromotolysis from fatigue; right, extreme retrograde chromotolytic degeneration. (*After Dolley*, 1913. *From J. F. Fulton. Physiology of the nervous system. 2d ed. New York: Oxford*, 1943. *P*. 39. *By permission of the publishers*.)

Electrical Methods. Neither the descriptive nor the degeneration methods are sufficient to reveal every aspect of the structure of the nervous system. Many fibers and sometimes even cell bodies are hard to see and trace; at least we cannot always know when the fibers have been cut or cell bodies have disappeared. Then, too, there are many parts of the nervous system in which cell bodies and fibers are not clearly separated into tracts and nuclei but are all mixed up together. Finally, many cells have very short axons and dendrites, which makes it difficult to trace their connections. In these cases there are two other methods that, used separately or together, reveal a good deal of desired information. One is the electrical method; the other is a chemical method.

Electrical methods have been improved a great deal in recent years and are coming into more frequent use. They usually have two aspects, stimulation and recording, but the most important part is the recording. Electrodes may be placed at any particular location in the nervous system. Then some other receptor, nerve, fiber tract, or nucleus may be stimulated, electrically or otherwise. If the point stimulated has some functional connection with the point at which the electrode is placed, nervous impulses will be picked up by the electrode and will appear in the recording instrument attached to the electrode. By varying the point of stimulation and the placement of the electrode, maps may be made depicting many types of connections in the nervous system. This technique is now proving extremely useful in telling us of connections in the nervous system which are important in physiological psychology but which were not discovered by the older descriptive and degeneration techniques (see Woolsey, Walter and Walter).

Chemical Method. These are ordinarily used in connection with electrical recording devices. Some chemical substance to which neurons are especially sensitive is put on a nerve or in some part of the nervous system. Electrodes are then placed in other parts of the nervous system to pick up impulses instigated by the chemical substance. The areas of the nervous system that are 'fired' in this way are shown to have connections with the place in which the chemical material was put. The substance that has been used most commonly for this purpose is strychnine, a drug to which the nervous system is extremely sensitive. The method of *strychninization*, as it is called, has proved very useful in mapping many of the connections and relations of the cerebral cortex of the brain and its closely allied structures (see Dusser de Barenne).

With this brief review of methods for studying the nervous system and its structure, let us now proceed to a review of its general structure and characteristics. The facts that we shall describe have been gained by several of the methods. Sometimes we shall mention them; sometimes we shall not. The methods, however, will also prove useful in later chapters when we deal with the specific topics of the senses and motor functions.

THE SPINAL CORD

As you have already read, the central nervous system consists of the brain and the spinal cord. The brain is, of course, the highest and most important center of integration. Some impulses come to it and leave it through the cranial nerves, but sensory impulses from all over the body except the head come to it through the spinal cord. Likewise the control of the actions of the body, except the face and neck, is exercised by the brain through conduction paths that lead through and out of the spinal cord. In the spinal cord, therefore, are to be found great conduction paths proceeding upward and downward between the brain and the various exits and entrances of the spinal nerves. Conduction is thus the first important function of the spinal cord. In addition, however, the spinal cord serves as an integrating center of its own and mediates, as we shall see in later chapters, many complex reflex actions without much help from the brain. But with this brief comment concerning its general function, let us turn to consider the essential anatomy of the spinal cord.

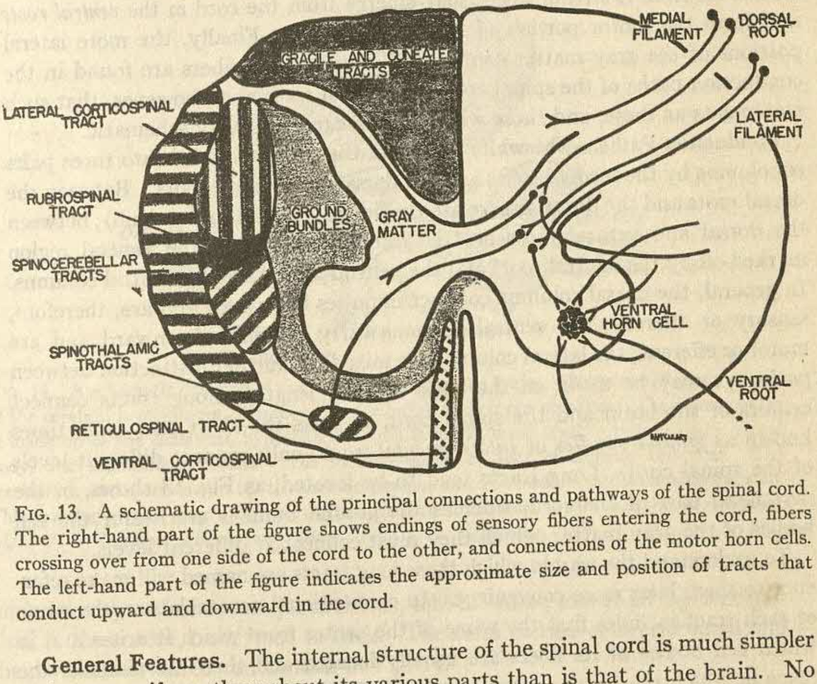

FIG. 13. A schematic drawing of the principal connections and pathways of the spinal cord. The right-hand part of the figure shows endings of sensory fibers entering the cord, fibers crossing over from one side of the cord to the other, and connections of the motor horn cells. The left-hand part of the figure indicates the approximate size and position of tracts that conduct upward and downward in the cord.

General Features. The internal structure of the spinal cord is much simpler and more uniform throughout its various parts than is that of the brain. No matter where it is sectioned, it presents the same essential appearance. The interior is gray matter (cell bodies), so distributed as to present the picture of a butterfly whose essential form is the letter H (see Fig. 13). Outside the gray matter are great columns of white matter making up various fiber tracts passing up and down the cord. Dividing the cord into two symmetrical halves are two median clefts, the dorsal and ventral fissures. Between them, in the central part of the cord, are two commissures joining the two halves of the cord; one is the crossbar of the H, composed of gray matter and called the *gray commissure;* ventral to it is the *white commissure*, which consists of fibers passing from one side to the other.

Gray Matter. The central parts of the gray matter are concerned mainly with impulses crossing the mid-line in commissural fibers, for there are fibers as well as cell bodies in the gray matter. The cell bodies of the more peripheral gray matter are concerned, on the other hand, with sensory or motor functions or with projection functions. Thus the dorsal horns of gray matter extend outward toward the edge of the cord to the point where the fibers of the dorsal sensory ganglion pass into the cord by way of the *dorsal root*. The dorsal horn is, therefore, in great part sensory in function. Although the ventral horn is not so near the surface of the cord, it is plain that its functions are mostly motor, for from it stream fibers that emerge from the cord in the *ventral roots* and form the motor portion of the spinal nerves. Finally, the more lateral portions of the gray matter contain cell bodies whose fibers are found in the conduction paths of the spinal cord. One must remember, however, that such statements as these, and those which follow, are necessarily schematic.

Conduction Paths. The white matter of the cord is divided into three pairs of columns by the median clefts and the dorsal and sensory roots. Between the dorsal roots and the dorsal fissure are the dorsal columns (or fasciculi); between the dorsal and ventral roots are the lateral columns; in the ventral region marked off by the ventral roots and the ventral fissure are the ventral columns. In general, the dorsal columns conduct impulses brainward and are, therefore, sensory or afferent; the ventral columns carry impulses downward and are motor or efferent; the lateral columns are mixed. A further distinction between pathways may be made on the basis of their length. Long tracts connect centers of the brain and the spinal cord, whereas the short ones, sometimes known as *ground bundles* or *intersegmental tracts*, only connect different levels of the spinal cord. Long tracts tend to be located, as Fig. 13 shows, in the peripheral part of the cord, whereas the ground bundles are nearer the cell bodies of the gray matter, which they must connect at different levels.

To understand the way in which these long tracts are named will make reference to them later more convenient. In conventional nomenclature, the name of each tract includes first the name of the center from which it arises and in which cell bodies of its fibers are usually located and then the name of the place in which the fibers of the tract end. There are a few exceptions to this rule; tracts are sometimes assigned special names according to their significance or according to the persons who first described them. Some of the more important tracts are named and related to each other in Fig. 13. These tracts will be referred to from time to time in later chapters, and the illustration accordingly deserves special attention. There is, however, no need for their further description at this point.

THE MYELENCEPHALON

Now we are going to proceed upward through the five main divisions of the brain. We have already named them briefly at the beginning of the chapter.

These five divisions have been selected by neuroanatomists because they can trace these divisions through the embryological development of the brain. Early in the growth of the brain there are only three simple divisions of the brain, which are easily seen as primary enlargements. They are then called the *forebrain*, *midbrain*, and *hindbrain* in embryological development. Later the forebrain divides into two parts, the *telencephalon* and the *diencephalon*. Nothing happens to the midbrain (*mesencephalon*), but from the division of the hindbrain arise the *metencephalon* and *myelencephalon*. Thus the adult brain is composed of five major divisions, tel-, di-, mes-, met-, and myelencephalon, in that order, from front to back. The main picture of development and the divisions involved can be seen in Fig. 14.

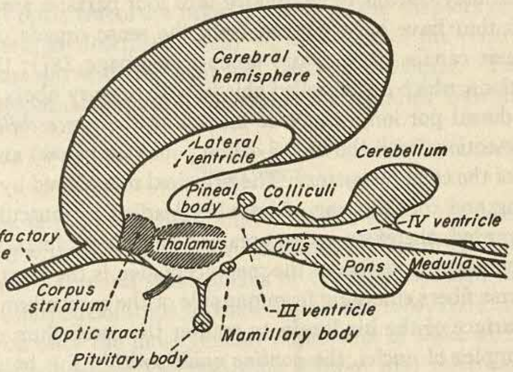

FIG. 14. A schematic drawing of the main divisions of the brain. The telencephalon consists of the cerebral hemispheres, olfactory lobe (or bulb), and corpus striatum. The diencephalon is made up of the thalamus, hypothalamus (not labeled), optic tract, pituitary body, pineal body, and mammillary bodies. The mesencephalon consists of colliculi and crus. The cerebellum and pons make up the metencephalon, and the medulla is the myelencephalon. This drawing gives a general scheme of the structure of the brain in all the higher vertebrates. (*After J. D. Lickley. The nervous system. New York: Longmans*, 1919. *P*. 20.)

The myelencephalon, which we shall take up first, is a relatively simple structure that is more commonly called simply the *medulla* (the adjectival form is *bulbar*). It joins the spinal cord to the higher centers of the brain. It is important as the place of exit and entrance of the majority of cranial nerves (see Fig. 8). As you might suspect, it contains several nuclei of cell bodies associated with these nerves. In addition, however, it contains autonomic nuclei concerned with breathing, heartbeat, and blood pressure. For this reason the medulla is sometimes called the vital center of the brain. Without it the fundamental processes of breathing and heart action could not go on. Finally, the medulla contains many tracts passing through it, which conduct impulses upward and downward between the cord and the higher centers of the brain. Later in this chapter, when we compare the brains of different animals, some of the functions of the medulla will be described in more detail.

THE METENCEPHALON

Going upward from the medulla, the second division of the brain, the metencephalon, consists of the cerebellum, the pons, and a part of the fourth ventricle. The cerebellum is a structure that resembles the cerebral hemispheres in that gray matter forms its outer surface and white matter, together with certain nuclei, makes up its interior. For purposes of brief description, the cerebellum may be said to be divided into four parts: a *ventral* portion, receiving fibers that have been relayed from the sense organs of equilibration, the semicircular canals, utricle, and saccule (see page 287); the *anterior* and *posterior* portions, which are supplied chiefly with sensory fibers from the spinal cord; and a dorsal portion, otherwise known as the *neocerebellum*, which has extensive connections with the nuclei of the pons (see below) and also with the frontal lobes of the cerebral cortex. The principal role played by the cerebellum is a smoothing and coordinating of impulses leading to muscular movements; it is to be regarded, therefore, as an organ of motor coordination.

Forming the ventral portion of the metencephalon is the *pons*. This consists of (1) transverse fibers emerging from one side of the cerebellum and traversing the ventral surface of the hindbrain to reenter the cerebellum on the opposite side; (2) a complex of nuclei, the *pontine nuclei*, within this band of transverse fibers; and (3) fiber tracts ascending and descending to various levels of the central nervous system. In the pons, also, are to be found the nuclei of the trigeminal nerve (Vth) which is so important in sensations and movement of the mouth and face.

MESENCEPHALON

The third division, the mesencephalon, is just as well called the *midbrain*. It is relatively small and forms a bridge or stalk connecting the forebrain and hindbrain. The main parts of the midbrain that interest us are the *tectum* (which means "roof") and the floor.

The floor is mainly a passageway between higher and lower parts of the nervous system. Sensory tracts run upward in it, and the motor tracts course downward. Also in the floor of the midbrain are some motor reflex centers that we shall consider at a later time.

The tectum of the midbrain, on the other hand, has sensory duties. The tectum is divided into two pairs of sensory centers—four in all. Each one is called a *colliculus*. One pair of such centers, called the *superior colliculi*, makes 'bumps' that lie a little above and ahead (anterior) of the other pair. The superior colliculi are primitive visual centers. The other pair of colliculi are called the *inferior colliculi* because they lie a little behind and below the level of the superior colliculi. The inferior colliculi are lower centers for hearing.

DIENCEPHALON

The diencephalon is one of the two divisions that, in evolutionary history, differentiated from the primitive forebrain. It is not so simple as some of the structures below it that we have been discussing. It has a number of parts: the thalamus, the optic tracts and retinae of the eyes, the pituitary body, the mammillary bodies, the hypothalamus, and the third ventricle. Of this list of parts, the pituitary body is a ductless gland that secretes hormones and will therefore be discussed in a later chapter concerned with internal secretions. The retinae and optic tracts are taken up later in the chapters on vision. The third ventricle will be described briefly with the rest of the ventricular system when we are through with the principal parts of the brain. That leaves the thalamus, the hypothalamus, and the mammillary bodies to be discussed here.

THALAMUS

The thalamus is the great relay station of the brain. It consists of many nuclei connected with each other, with the lower centers of the brain and spinal cord, and with the cerebral hemispheres of the telencephalon above it. The structure and interrelationships of these nuclei are most difficult to visualize. We can give you only the most general impression of them at this point. It is impossible to talk about the thalamus without also referring to the lobes and parts of the cerebral cortex lying above it. The explanation of these references will come along when we discuss the telencephalon in the section following this one.

Subcortical Nuclei. We can divide the nuclei in the thalamus into three main groups. Nuclei with only subcortical connections are disposed mainly along the mid-line of the thalamus and in the anteroventral part; they connect in some cases with the basal ganglia or with other parts of the thalamus, but so far as is known they do not send any fibers to or receive any fibers from the cerebral cortex. They are of little significance to us.

Relay Nuclei. A second group of nuclei, the thalamocortical projection nuclei, otherwise known as the *sensory relay nuclei*, are of the greatest importance (see Figs. 15 and 16). Of this group we need mention only the ones with which we shall come in contact most often. The *lateroventral nucleus*, lying in a position indicated by its name, receives fibers from the cerebellum and sends projections to the frontal lobe, particularly the precentral gyrus. It functions, as one might suspect from its anatomical connections, in the coordination of the activities of the cerebellum and the frontal lobe in controlling muscular movements. The *posteroventral nucleus*, situated close to the lateroventral, is the major relay station for sensory fibers representing the skin and muscle senses and sends projections to the cortex, particularly to the postcentral gyrus, which is employed in somesthetic sensory activities. Besides these two parts of the ventral nucleus, there are two other thalamic relay nuclei of note, the *lateral* and *medial geniculate bodies*, which are slight enlargements on the lateral surface of the thalamus. The former is the station through which impulses from the eyes are relayed to the cortex and to other visual centers, whereas the latter exercises a similar function in hearing. Of these two centers you will read much in later sections.

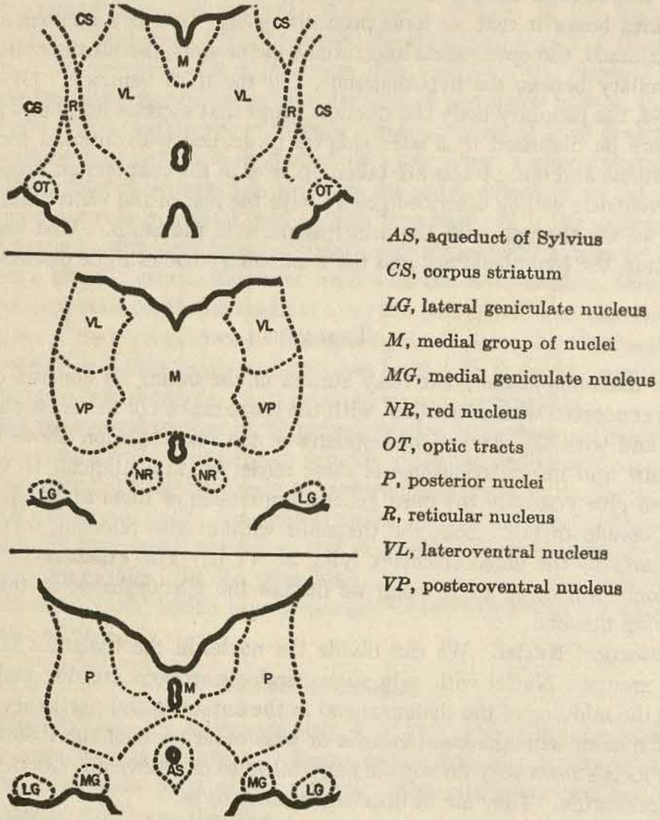

FIG. 15. Three diagrammatic cross sections of the thalamus showing its principal nuclei. The upper section is from the anterior thalamus, the middle section is from the middle thalamus, and the lower section is from the posterior thalamus. For context, the corpus striatum (*CS*), reticular nucleus (*R*), optic tracts (*OT*), and red nucleus (*NR*), none of which are part of the thalamus, are shown in the upper or middle section. The main nuclei of the thalamus are the medial group (*M*), the lateroventral nucleus (*VL*), posteroventral nucleus (*VP*), the posterior group of nuclei (*P*), the lateral geniculate bodies (*LG*), and the medial geniculate bodies (*MG*). See Figs. 16 and 112 for other relations of some of these nuclei. (*Based on Fulton, p.* 256, *and Walker.*)

Association Nuclei. The third group of thalamic nuclei are the 'association' nuclei, which receive their impulses from within the thalamus but send projections to the cerebral cortex (see Figs. 15 and 16). In general, nuclei of this type send their thalamocortical fibers either to the anterior part or to the posterior part of the cortex. The particular areas that they serve can only be understood by knowing something about the organization of the cortex, which we have not yet considered.

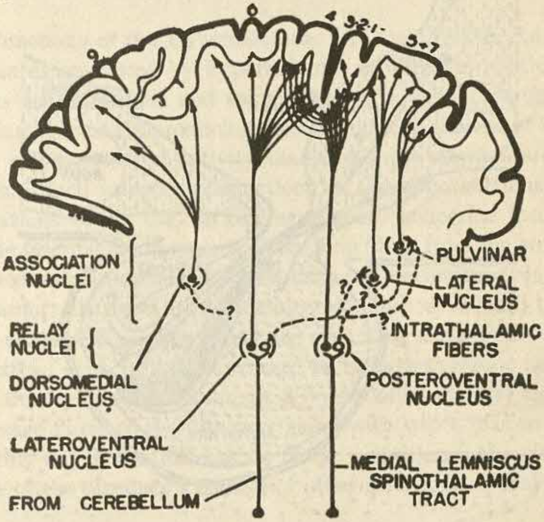

FIG. 16. Some projections of thalamic nuclei to the cerebral cortex. The dashed lines go to the association nuclei; those shown are the dorsomedial nucleus, the lateral nucleus, and the pulvinar. The solid lines in the center are the pathways of relay nuclei; those shown are the lateroventral and posteroventral nuclei. To keep the diagram as simple as possible, the visual and auditory projection systems are not represented in the figure. The numbers at the top of the figure refer to areas of the cerebral cortex. (*Based on work of Walker and Clark. After Ruch and Kasdon, unpublished.*)

THE HYPOTHALAMUS

The other principal part of the diencephalon is the hypothalamus and its associated structures. These, as you will see, have some important and unusual functions connected with the peripheral autonomic system. These functions set them apart from the other structures of the brain that we have been discussing.

Autonomic Nuclei of the Hypothalamus. Primary control of autonomic functions is vested in the hypothalamus. It is there that differentiation and organization of different patterns of autonomic reaction takes place. As one can see in Figs. 14 and 17, this center is rather clearly set off from the rest of the brain, lying in the ventral and medial part of the diencephalon. Associated with the hypothalamus is the pituitary gland and its stalk, the infundibulum, which projects from the floor of the hypothalamus (see Fig. 17). Also protruding from the floor of the hypothalamus are the paired *mammillary bodies* and the *tuber cinerium*. The rest of the hypothalamus proper is made up of several nuclei, which we may consider in two main groups: (1) the posterior and lateral nuclei, and (2) the medial and anterior nuclei. The function of the former is primarily sympathetic, whereas the latter organize, for the most part, parasympathetic functions.

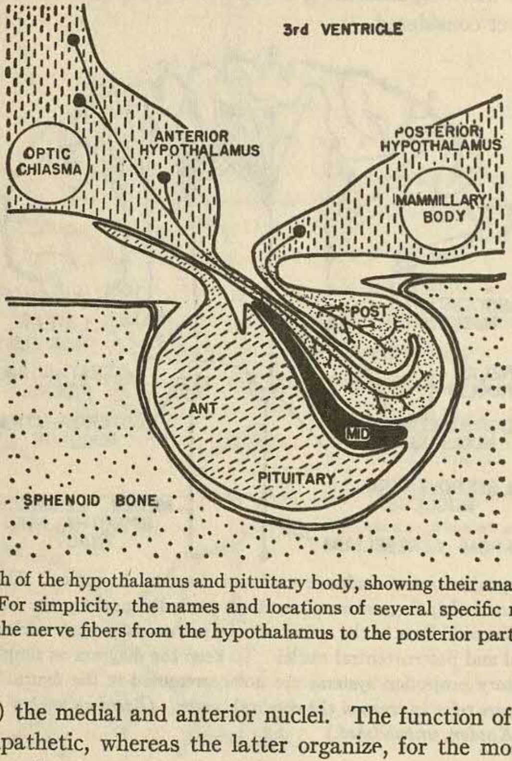

FIG. 17. A sketch of the hypothalamus and pituitary body, showing their anatomical relations to each other. For simplicity, the names and locations of several specific nuclei have been omitted. Note the nerve fibers from the hypothalamus to the posterior part of the pituitary body.

If one stimulates the first, or posterior, group electrically, all the effects of sympathetic discharge are obtained: the pupils dilate, the heart is accelerated, blood pressure is elevated, stomach contractions and intestinal activity are halted. Removal of this group of nuclei presents all the symptoms of lessened activity of the sympathetic system and of a resulting dominance of parasympathetic activity: the pupils contract, the heart beats slower, the blood pressure drops. Moreover, the result of extirpation of the mammillary region of the hypothalamus, which makes up part of the posterior group of nuclei, is abnormal sleepiness or somnolence. As we shall see later (Chap. XVII), sleep is under the influence of the parasympathetic system, and it is therefore reasonable that removal of the sympathetic centers should serve to induce it.

The anterior and medial group of hypothalamic nuclei is predominantly parasympathetic in function. If it is stimulated electrically, the heart is slowed, blood sugar is lowered, and various other parasympathetic phenomena appear. To destroy the anterior group is to bring about an increase in blood sugar, a rise in heartbeat and blood pressure, vasoconstriction, and general sympathetic effects. These are the results to be expected if the sympathetic system is left without the antagonistic effect of the parasympathetic division.

General Functions of the Hypothalamus. All the individual autonomic effects that can be produced by hypothalamic activity are controlled also by lower centers in the medulla and spinal cord. The distinctive importance of the hypothalamus is not in producing these autonomic effects but in its *integration* of them into patterns of activity that adjust the internal environment of the organism. Such integrating functions of the hypothalamus are derived from its relations to all the various neural and endocrine mechanisms for regulating the internal environment. Receiving fibers from the cerebral cortex, it makes autonomic adjustments appropriate to the cortical events mediating somatic behavior. It sends efferent projection fibers downward to the bulbar mechanisms of respiration, heartbeat, and glandular regulation. Such projection fibers extend even farther downward to the preganglionic neurons of the spinal cord, thus regulating autonomic adjustments. Finally, the hypothalamus sends nerve fibers to the pituitary gland with which it is so closely associated. In this way it controls certain of the activities of the pituitary gland and, because of the pituitary's control of other glands, hormonal secretions in general.

We may note in passing some of the general functions that the hypothalamus is able to subserve by these various means. Body temperature is crucially dependent upon this center. Whenever it is necessary for the body to lose heat, the hypothalamus causes vasodilation, increased sweating, increased respiration, and a lowering of metabolism. Through converse effects it causes heat to be conserved, and in addition, by inducing shivering, the body temperature to be raised. As the primary neural center regulating endocrine secretions, the hypothalamus plays a major role in regulating metabolism, particularly of fats, carbohydrates, and water. It is there, too, that the control of blood pressure and thus of the distribution of blood to the brain is mainly, though not exclusively, vested. Sexual functions, which include complex autonomic effects (see Chap. XX) as well as certain somatic reactions, depend upon the hypothalamus. Furthermore, physiological conditions associated with hunger and thirst are dependent in an important degree upon the activity of the hypothalamus. That it is also a center for emotional behavior will be shown in some detail in a later chapter. There is, therefore, a long list of important activities of the hypothalamus—more perhaps than one would expect to be contained in a neural center that is comparatively so small.

TELENCEPHALON

This consists of the olfactory bulb and olfactory tracts, the cerebral hemispheres, the lateral ventricles, and the basal ganglia.

The Olfactory Bulbs. These lie in the anterior region of the cranial cavity immediately above the olfactory receptors (see Fig. 14). They are made up principally of cell bodies which are connected with the brain by the fibers of the olfactory nerve terminating on the ventral surface of the brain.

The Cerebral Hemispheres. These consist of the cerebral cortex (meaning "rind" or "covering"), which is gray matter; white fiber tracts, which underlie the cortex and pass between it and lower parts of the brain; and the corpus callosum, which is made up of fiber tracts passing between the cortices of the two cerebral hemispheres.

Of these, the cerebral cortex will receive a large measure of our interest, for in it reside the complex psychological functions that distinguish man. In birds and lower animals the cortex is not very important; only the first signs of its development are present. In mammals, however, the cortex undergoes a great development compared with changes in the rest of the nervous system. Indeed, in man the cerebral cortex is about one-half the weight of the entire nervous system, and it has so expanded into its allotted space in the skull that it shows many invaginations and ridges which thus greatly enlarge the amount of cortex. An invagination has the name *sulcus* or *fissure*, and the ridge between two of them is known as a *gyrus*.

To indicate various parts of the cerebral cortex, one makes use of certain sulci and gyri as landmarks, the most important being described here. The cortex is divided into two symmetrical halves, or hemispheres, by the deep *longitudinal fissure* that runs along the mid-line. On the dorsal surface of the cortex and somewhat posterior to the center is the *central sulcus*, a deep furrow that runs laterally and slightly anteriorly from the median longitudinal fissure. On the lateral surface of the cortex the *lateral fissure* may be seen running posteriorly and dorsally.

Lobes of the Cortex. On the basis of these three principal fissures, one may mark off four pairs of lobes in the cerebral cortex (see Fig. 18). The *frontal lobes* include all the cortex anterior to the central sulcus. The *parietal lobes*, occupying the dorsal surface of the hemisphere, extend posteriorly from the central sulcus and laterally to the lateral fissure. Lateral and ventral to the lateral fissure, one finds the *temporal lobes*. A fourth pair of lobes, the *occipital*, are also distinguished, but they are not marked off by any major fissures (Fig. 18).

Architectonic Structure. The cerebral cortex can also be described in terms of its histological, or cellular, structure. Although the cortex is really a great ganglion, it is unlike most ganglia found elsewhere in the nervous system in that, possessing as it does a great many connections between its various cells, it also contains a great number of nerve fibers. A large proportion of the cortical cells, in fact, possess comparatively short and greatly branched fibers which connect only with other cells within the cortex. Moreover, there are different kinds of cells, as well as connections, and the study of these, by means of appropriate histological techniques, brings out systematic differences in the organization of cells in different cortical areas.

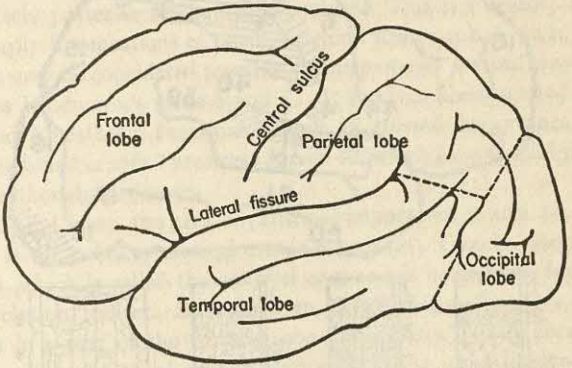

FIG. 18. Side view of the human brain showing lobes and principal fissures and sulci that are used to describe the position of various areas of the cerebral cortex. (*From A. Kuntz. A textbook of neuroanatomy. 4th ed. Philadelphia: Lea & Febiger,* 1945. *P.* 335. *By permission of the publishers.*)

Such a study of cytoarchitecture has yielded several facts of importance (see Fig. 19). It has shown us, first of all, that the cortex is composed of six fundamental layers. Within these layers there may be subgroups, and some layers may be more or less prominent in certain areas, but the entire cortex has the same essential structure in this respect. We need not now go into the anatomical details of these layers.

Areas of the Cortex. Of importance, however, is the fact that the ridges of the cortex differ in cytoarchitectural structure and that these differences are in some degree correlated with diverse functions. For this reason and also for convenience in specifying precisely particular areas of the cortex, systems of denotation of various cytoarchitectural areas—*i.e.*, areas differing in the characteristics of the six layers—have been worked out. A widely used system, developed by Brodmann, is shown in Fig. 19 and is the one used in this book whenever we have need of such a system.

Let us briefly discuss the relation of the cytoarchitectural areas to the four lobes described above and to their general psychological functions. Within the frontal lobes we may distinguish four principal areas as we go from the central sulcus to the anterior pole of the hemispheres. (1) The *precentral area*, immediately in front of the central sulcus, is the electrically stimulable area discovered by Fritsch and Hitzig, often called the *motor area* or *Brodmann's area 4.* (2) Immediately in front of it is the *intermediate precentral area*, sometimes called the *premotor area* or *Brodmann's area 6*, which is intimately

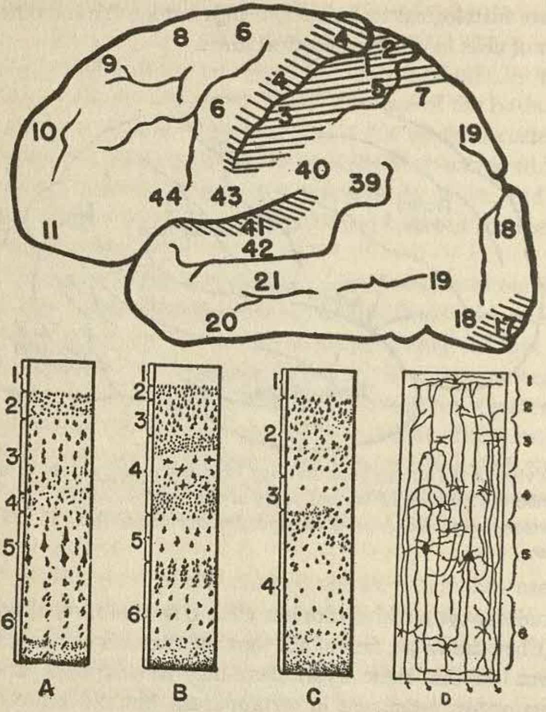

FIG. 19. A schematic drawing of Brodmann's areas of the cortex and the cellular layers of different areas. The numbers in the upper part are those of cortical areas in the Brodmann system, and those below are numbers of the layers of the cortex. *A* below is a cross section from area 4 above, which is a motor area; it shows that layer 4 is relatively very narrow and layer 5 is rather prominent. *B* is from area 17 above, which is the visual area of the cortex, and it has a highly developed layer 4 and a rather thin layer 5. *C* is from the medial and ventral portion of the temporal lobe, which is made up of olfactory cortex (paleocortex); it illustrates the fact that primitive cortex has only 4 layers. *D* is a diagram of synaptic relations in area 4 as seen in silver staining and indicates that synaptic connections are mainly radial, *i.e.*, from one layer to another, rather than horizontal, *i.e.*, within the parts of the same layer. (*From S. Cobb. Foundations of neuropsychiatry. Baltimore: Williams & Wilkins,* 1941. *P.* 72. *By permission of the publishers.*)

concerned in motor functions. Lying at the foot of this premotor area and having a somewhat different cytoarchitectural structure is an area important in speech. Its function was discovered by Broca and so the area sometimes bears his name, but it has the number 44 in Brodmann's system. Occupying the larger and anterior part of the frontal lobe are the (3) *prefrontal areas*, sometimes referred to as the frontal "association" areas because they seem to have special importance in integrating mental activity. They are made up of a number of different architectural areas with their respective numbers (see Fig. 19). In the present study, however, we shall usually consider the areas as a whole by names rather than by numbers.

In the parietal lobe there is first the *postcentral area*, Brodmann's 3-1-2, which lies immediately posterior to the central sulcus. This is a sensory area, concerned primarily in sensations of touch. Behind it are several areas, which for our purposes may be considered together as the *posterior parietal area* or lobule. This includes Brodmann's areas 5 and 7. It receives fibers related indirectly to touch and kinesthetic functions and is of proved importance in them. Sometimes included in area 7 are areas 39 and 40, which have special significance in the higher thought processes.

In the occipital lobes, the area of principal importance is area 17, the *striate area*, which is the primary cortical center for vision. Closely associated with it is area 18, which is called the *occipital area* and is believed to function as a visual "association" center. So also is area 19, which is really not in the occipital lobe but is a part of the parietal lobe and of area 7; but because it has connections with subcortical centers that seem to be visual in function, it is grouped with areas 17 and 18 as concerned in visual functions.

A considerable part of the temporal lobe requires no specific denotation. Only two areas need be pointed out. A primary sensory area concerned in hearing is to be found lining the walls of the lateral fissure and is numbered by Brodmann as areas 41 and 42. Close by it is the audiopsychic area, so called because it is held to be an "association" area for hearing.

Fibers of the Cerebral Hemispheres. Below the cerebral cortex is a great mass of nerve fibers of which a large part are myelinated, therefore constituting white matter. These fibers are of three kinds: *commissural*, *association*, and *projection* fibers. Those of the first type have their cell bodies in the cortex of one hemisphere and pass in a great white sheet to the other hemisphere. These fibers make up the *corpus callosum*, which is the principal connection between the two hemispheres and forms the floor of the median longitudinal fissure as well as the roof of the lateral ventricles (see below). Besides the corpus callosum there are other commissural fibers passing between the two hemispheres, but they are of little concern to us.

'Association' fibers are those which connect one part of the cortex to another. They were formerly thought to play a large part in the integration of activities of the cortex, but it now appears that they do not extend very far from their points of origin, and it is more probable that the relation of various areas to each other is conducted directly through the cortex or by way of the thalamus.

Of greatest functional importance are the projection fibers by which impulses get to and leave the cortex. Projection fibers are classified as *afferent* or *corticopetal* (those radiating upward from the thalamus and other subcortical centers to the cortex) and *efferent* or *corticofugal* (those projecting downward to various subcortical centers). These latter fibers may end at any one of several points: the basal ganglia, thalamus, midbrain, hindbrain, or ventral cells of the spinal cord. Corticopetal fibers, on the other hand, take their origin almost without exception in the nuclei of the thalamus. How such nuclei are related to areas of the cortex will be considered in some detail below.

The Basal Ganglia. The phylogenetically oldest parts of the telencephalon are the basal ganglia. These are a mass of gray matter lying below the cortex and, for the most part, above the thalamus or diencephalon, although certain small but important parts of them are lodged between the diencephalon and mesencephalon (midbrain). These latter, the *substantia nigra* and the *red nucleus* (see pages 285 and 307), are of great significance in the maintenance of the posture of the organism and in certain aspects of the coordination of movement. Although properly a part of the cerebral hemispheres, they appear to have migrated, in phylogenesis, away from the main portion of the basal ganglia, which is the *corpus striatum*. This term means "striped body" and has its origin in the fact that projection fibers passing upward and downward between the cortex and thalamus are interspersed among the cell bodies of the corpus striatum, thus giving it its striped appearance. The corpus striatum is a fairly complex as well as important structure, but its further description is not necessary for the present purposes (see Chap. XIII).

CEREBROSPINAL FLUID

In talking about the various parts of the brain above, we have frequently mentioned the ventricles. A word is in order about what these are, how they are arranged, and what they contain.

All organs of the body are supplied with blood in greater or lesser amounts, and the nervous system, because of its crucial importance in the economy of the body, receives much more than most other organs. Peculiar to the nervous system, however, is another type of fluid supply, the cerebrospinal fluid. This is to be found in the *ventricular* and *subarachnoid* cavities of the brain and spinal cord. The ventricular system is within the brain and spinal cord, the subarachnoid spaces are in the external linings.

The ventricular system consists of four ventricles in the brain and a spinal canal in the spinal cord. Two ventricles, ordinarily called the *lateral ventricles*, are to be found in the cerebral hemispheres in a position indicated back in Fig. 14. These communicate with each other and with the third ventricle, which is located in the mid-line in the thalamus and hypothalamus. By means of the Sylvian aqueduct which passes through the midbrain, separating it into a floor and a roof, the third ventricle is connected with the fourth ventricle contained within the posterior pons and anterior medulla. This narrows down in the posterior part of the medulla to a small canal which runs the length of the spinal cord in the gray commissure.

The subarachnoid spaces are between layers of the external lining of the brain (meninges). One of them comes into close proximity with the fourth ventricle, being separated from it only by a thin membrane, which has small openings in it through which fluid from the ventricular system can communicate with that in the subarachnoid spaces.

The cerebrospinal fluid is an almost colorless liquid very much like the blood in composition except that it has no red or white corpuscles and contains no blood proteins. Indeed, it appears to be rich in the food materials of the blood. Its function with respect to the nervous system is not clearly understood, although it is clear that it is partly nutritive. It is widely believed that this fluid is secreted or filtered from the blood in networks of arterial blood vessels (choroid plexi) found in the ventricles, and it appears to be absorbed by a similar net of venous vessels (arachnoid villi) in the subarachnoid spaces. The importance of the cerebrospinal fluid in understanding nervous functions rests at present on certain correlations between changes in its chemical constitution and changes in nervous function and also on the effect upon nervous activities of alterations in its pressure.

EVOLUTION OF THE BRAIN

We have now run over quickly the main parts of the central nervous system with some brief mention of the function of these parts. There will be considerably more detail later in connection with specific topics. But before we leave this general review of the central nervous system, it would be well to consider it from an evolutionary point of view.

What we have been talking about is a typical brain of one of the higher mammals, such as a monkey or ape or man. Actually the description would not be far off for the cat or the dog. The essential structure of the central nervous system, however, began in the lower vertebrates, and this in turn had its origins in invertebrate evolution. It will help us, therefore, to understand some of the functions of the parts of the nervous system, as well as to fix more clearly in mind what we have already discussed, if we run over briefly some of the principal features of the evolution of the central nervous system.

Invertebrates

First let us look at the fundamental characteristics of nervous structure and function which have been laid down in invertebrate evolution. These are rooted, as we have already seen, in the differentiation of effectors, receptors, and adjustors. The adjustors, we know, make up the nervous system. This in its most primitive form is the *nerve net*, found in members of the phylum

Coelenterata (*e.g.*, the jellyfish). The nerve net appears to be a syncytium of several nerve cells and therefore to possess no true synapses (page 67). Conduction in the nerve net, consequently, is diffuse and is not provided with the differentiation of pathways with which a synaptic nervous system is endowed.

Pattern of Organization. After the nerve net came two important steps in nervous development. (1) The syncytium was dropped, and in its place arose nerve cells that could act in some measure independently of each other. Here was established the basis for the organization of the nervous system into centers and pathways. (2) The nervous system came to be gathered into one part of the organism, the part depending upon which of two organismic patterns was developed. In the echinoderms (*e.g.*, the starfish) the organismic pattern was *radial*, with the nervous system accordingly disposed in a radial pattern, its center a concentric ring of nervous tissue placed at the hub of the animal with its nerves radiating out to the periphery. Evidently the radial pattern was incapable of further differentiation, for it never went beyond the rudimentary form found in echinoderms. A second type of organismic pattern, the *axial*, is the one that has been preserved throughout subsequent invertebrate and vertebrate evolution to man. In this we find the body and the nervous system organized along an anteroposterior axis—from the head to the tail. Examples of it will be presented below.

Ganglionic Organization. Accompanying the evolution of the axial form of nervous system is the development of another characteristic, which becomes more and more important in later evolution—*ganglionic organization*. In worms it is not very highly developed; a chain of ganglia is arranged in pairs along the axis of the body, each pair serving a segment of the body in such a way that the nervous system takes the form of a ladder. In other animals, such as the insects, the general tendency is to bring each pair together into one ganglion located in the axis of the body and to reduce the number of ganglia, with the result that the major ganglia tend to be distributed according to the major divisions of the body, *i.e.*, head, trunk, abdomen—although smaller ganglia located according to the segmentation of the body do not entirely disappear. In vertebrates the major ganglia are still further reduced in number to one, thus forming a unified central nervous system; yet the representation of the segments of the body is still retained in greater or lesser degree.

VERTEBRATES

The later stages of nervous evolution, to be found mainly, although not exclusively, in the vertebrate series, display a fourth important feature—*encephalization*: the major ganglion, which in vertebrates is the brain, comes to be located in the head end of the organism. More than that, however, in encephalization the head ganglion has taken over more and more of the integrative and controlling functions of the posterior nervous system. Still later, with the emergence of the cerebral cortex, *corticalization* of functions, in which functions are transferred from lower parts of the brain to the cortex, is the important trend in nervous evolution. These major trends are illustrated in Fig. 20.

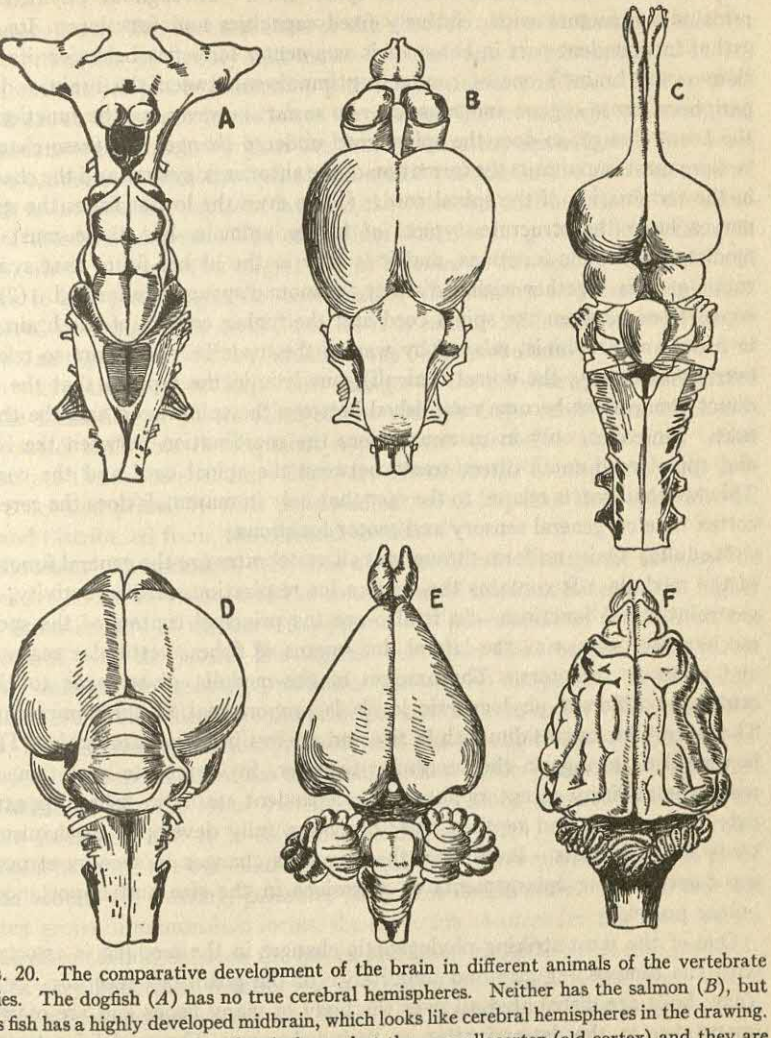

FIG. 20. The comparative development of the brain in different animals of the vertebrate series. The dogfish (*A*) has no true cerebral hemispheres. Neither has the salmon (*B*), but this fish has a highly developed midbrain, which looks like cerebral hemispheres in the drawing. The alligator (*C*) has cerebral hemispheres, but they are allocortex (old cortex) and they are relatively small. In the pigeon (*D*) we see a comparatively large cerebral cortex, but only in mammals like the rabbit (*E*) do the hemispheres make up the major portion of the brain and consist primarily of neocortex (new or somatic cortex). In the dog (*F*) the hemispheres are still larger, and they begin to crease and fold in convolutions. (*After Wiedersheim. From P. H. Mitchell. A textbook of general physiology. 4th ed. New York: McGraw-Hill,* 1948. *P.* 161. *By permission of the publishers.*)

The Spinal Cord. Turning now to more detailed aspects of vertebrate evolution, let us take up each of the major parts of the nervous system and note the changes in both structure and function that have taken place in phylogenesis. First to be considered is the spinal cord. Throughout phylogeny it remains a structure with relatively fixed capacities and functions. Its own rather independent part in behavior is as a center for reflex behavior; its relation to the brain is one of conducting impulses between the brain and the peripheral sense organs and muscles. In so far, however, as the functions of the brain change, so does the spinal cord undergo change. Of these changes, two are most important: the formation of the autonomic system and the changes in the termination of the spinal cord. (1) In even the lowest fishes the spinal nerves have the structure typical of higher animals, but these must also mediate autonomic functions, and it is only in the higher fishes that sympathetic ganglia together with a distinct autonomic system are formed. (2) All connections between the spinal cord and the higher centers of the brain are, in fishes and amphibia, relayed by way of the medulla. Some are so relayed even in man (*e.g.*, the dorsal funiculi); but it is in the reptiles that the first direct connections become established between the spinal cord and the thalamus. Moreover, only in mammals does the coordination between the brain and spinal cord entail direct tracts between the spinal cord and the cortex. This, we shall see, is related to the fact that only in mammals does the cerebral cortex take on general sensory and motor functions.

Medulla. Quite uniform throughout all vertebrates are the general functions of the medulla. It contains the centers for respiration, cardiac activity, and gastrointestinal functions. In it also are the principal centers of the special mechanoreceptors, *viz.*, the lateral line organs of fishes, vestibular receptors, and auditory receptors. The amount of the medulla given over to these centers at different phylogenetic levels is proportional to their importance. The lateral line organs diminish in size and are lost in higher amphibia. There is very little change in the vestibular receptors in vertebrate evolution, and while the auditory receptors have no independent status in fishes, appearing only in amphibia and reptiles, they become a fully developed mechanism in birds and mammals. Paralleling these various changes in sensory structure are corresponding enlargements or recessions in the size and importance of bulbar nuclei.

One of the most striking phylogenetic changes in the medulla is associated with the diminishing size and importance of the gustatory receptor system. Taste buds are distributed all over the body of many fishes and are of prime importance in the determination of their behavior. The nuclei for taste in the medulla are accordingly enormously expanded, so much so that they form large evaginations called the *vagal lobes*—*vagal* because they represent primarily the enlargement of the nuclei of the vagus nerve. The taste receptors are curtailed, however, in further evolution, and in mammals they are limited to the tongue and a small part of the internal surfaces of the mouth. With this recession of taste goes a diminution in the vagal lobes, until in man, for example, the gustatory nucleus becomes a comparatively inconspicuous center in the medulla.

Cerebellum. The first structure of the nervous system to be specialized for the coordination of sensory and motor impulses was the cerebellum. It was apparently developed in connection with the vestibular and lateral line systems which are so important in the lower vertebrates, but even in cyclostomes, prevertebrate organisms lower than the fishes, where the cerebellum is first seen, it has connections with the frontal and spinal portions of the nervous system. Much of its later development involves the extension and increase in the number of these connections. The cerebellum achieves its greatest importance in birds, where it reaches its largest size in relation to the rest of the brain and where it is a great organ for coordinating the sensory and motor impulses involved in flying. The cerebellum, as it is seen in birds and lower forms, is known as the *paleocerebellum*, which means "old cerebellum."

In mammals, the most important changes in the nervous system are related to the formation of the cerebral cortex and the large cerebral hemispheres. Associated with this development appear new cerebellar structures, which constitute the neocerebellum. These are the cerebellar hemispheres, and they are concerned primarily with the coordination of impulses that are delivered to, and distributed from, the cerebral cortex.

Midbrain. The principal functions of the midbrain throughout the phyletic series are audition, vision, and the conduction of impulses between the higher and lower centers of the nervous system. In fishes some of the midbrain is concerned with the lateral line organs, but when these organs disappear in higher animals the associated midbrain centers also disappear. In inframammalian forms the colliculi are the principal sensory centers for vision and audition, but as encephalization proceeds and the cerebral hemispheres are developed, the importance of the midbrain in these sensory functions diminishes.

Thalamus. In the lower vertebrates the thalamus constitutes almost the entire forebrain, and it is concerned principally with vision, forming relay stations between the eyes and the midbrain. It subsequently enlarges to include centers for hearing, pressure, pain, and temperature. As the cerebral cortex grows in mammalian forms, the thalamus becomes for the most part a great relay station between the cortex and lower centers, but it also probably serves very important functions as a coordinator of sensory impulses and of impulses traveling between it and the cortex. In warm-blooded animals, birds and mammals, the hypothalamus is differentiated from the main body of the thalamus and becomes an important center of integration for the autonomic system.

Corpus Striatum. This is established as a motor center in fishes. It expands greatly in amphibia and reptiles and reaches its greatest development in birds.

The cerebral cortex of the mammal takes over many of the functions of the corpus striatum, and as a result the latter becomes relatively less important in the later stages of phylogenesis.

The Cerebral Cortex. In fishes there exists no cerebral cortex; only the olfactory bulbs and a primitive forebrain, made up of thalamus and corpus

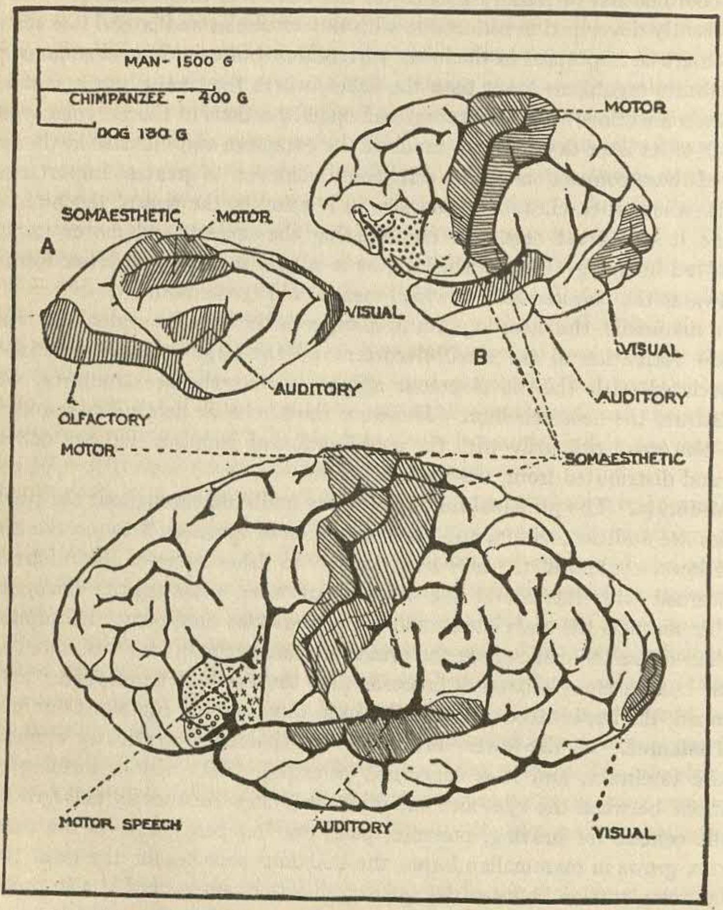

FIG. 21. Side views of three mammalian brains drawn to scale to show the relative sizes and degrees of development of the cerebral cortex. The positions and sizes of the primary sensory and motor areas are indicated approximately. Notice the increase in convolutions and the increase of cortical "association" areas not concerned in sensory and motor functions. *A*, the dog; *B*, the chimpanzee; and *C*, man. (*After Campbell. From G. W. Bartelmez. Man from the point of view of his development and structure. In H. H. Newman (Ed.), The nature of the world and of man. Chicago: University of Chicago Press,* 1926. *P.* 466. *By permission of the publishers.*)

striatum, are present. In amphibia and reptiles, however, a primitive cortex appears in the form of a nucleus of cell bodies interposed between the olfactory bulb and the rest of the forebrain; this first cortex is plainly concerned only with olfactory functions. Later on, in birds, is laid down the first cortex having nonolfactory functions, but only in mammals does it become a true cortex with a definite cortical structure as well as important functions. Such a "somatic" cortex is sometimes called *neocortex* because of its more recent phylogenetic development. One can distinguish it even in mammals from the old cortex, or *paleocortex*, which has olfactory functions. As olfaction recedes in importance in the adjustments of the animal and as various other sensory and motor functions become corticalized, the neocortex comes, in mammals, to constitute the larger and more significant portion of the cerebrum.

But above and beyond these basic stages in the evolution of the cerebral cortex are other important developments in the somatic cortex itself. Chief of these are the enormous growth and convolution of the cortex and the special prominence given to frontal-lobe development; these begin with the rat and reach their peak in man (see Fig. 21). The rat, for instance, has a very simple cortex with no convolutions, but in carnivora (*e.g.*, cats and dogs) one can observe clearly the principal fissures, the central and lateral, and the beginnings of others. In the primates and man, many fissures are present, forming numerous gyri by means of which one can denote rather precisely various parts of the cortex. The emergence and growth of a convoluted cortex goes hand in hand with increasing mass and with differentiation of both structure and function.

Worthy of special attention is the prominence given to the frontal lobes in such cortical development. In rats we are able to distinguish no true frontal lobes; only certain of the functions that reside in the frontal lobes of higher animals are found to be localized roughly in the frontal areas of the rat's brain. In carnivora and higher animals, however, the central fissure comes to set off these areas and functions from the rest of the brain. These areas which make up the frontal lobe, moreover, expand enormously in size and also quite obviously in the importance of the functions that they mediate. The size and prominence of the frontal lobes are, in fact, the most distinguishing characteristics of the brains of the carnivora and primates.

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CHAPTER IV

NERVE PHYSIOLOGY

In the last two chapters we have been concentrating on the structural characteristics of the response mechanism, how the receptors and effectors differ in basic structure, and how the central and peripheral nervous systems are arranged. Only incidentally, in order to help with the description of structures, did we mention general functions of the response mechanism.

Now, however, in order to understand how the receptors, effectors, and nervous system work, there is a great deal to be said about the processes which go on in them. To say it, we must go back again to the cell, for as we have pointed out before, cells are the fundamental units of all biological activities. In particular, we should pay especial attention to the nerve cell, or neuron. The properties of individual neurons and of many neurons in combination with each other are basically the properties of the nervous system. When we have covered neurons thoroughly, we have also told most of the story about receptors and effectors, for these function much like neurons in all except very specialized aspects of their activities. This chapter, then, is to be devoted to the physiology of neurons.

This subject is one in which research workers are very active at the present time. Hundreds of papers are being published every year, each furnishing us with new facts and ideas about how neurons work. There are still many unsolved problems in nerve physiology, and there are several points on which research workers differ. In a brief chapter, such as this one, about such a large and changing subject, we cannot possibly give you a completely accurate statement of its present status. We can only paint a general picture, which may turn out to be incorrect in certain details, but which nevertheless gives the general sense of present-day understanding of neuron functions.

POTENTIALS IN NERVE FIBERS

The typical structure of the neuron has already been described. It has a cell body and two types of fibers, the dendrites and the axon. It has a membrane and sometimes, but not always, a sheath around its fibers called the myelin sheath. As we shall see in the course of this chapter, there are some differences in the physiology of the fiber and of the cell body. To make the story an orderly one, we shall take up the fiber and its physiology in this section, then proceed later in the chapter to consider the special physiological features of the cell bodies and the neuron networks found in the central nervous system.

Our principal concern here will be the way in which nerve fibers are excited by stimuli and conduct their excitation throughout their lengths. The mechanism of excitation, as you will see, is inextricably tied up with various electrical potentials and currents in the fiber. Thus the story as we shall tell it will include some explanation of the potentials found in the nerve, how they lead one to another, and how they take part in the excitation and conduction of nerve fibers (see Lloyd, Eccles). The first point in the story concerns the resting potential of a nerve fiber.

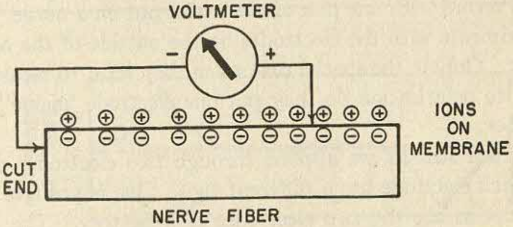

FIG. 22. Diagram of a polarized membrane and measurement of resting potential. Positive ions are on the outside and negative ions on the inside of the membrane of the nerve cell. These make a resting potential across the membrane, which can be measured by hooking up a voltmeter with one electrode at the cut end of a nerve fiber and the other on the outside of the fiber.

The Resting Potential. We have already seen that the membranes of cells can become polarized with more ions of a particular type, positive or negative, on one side of the membrane than on the other. Such polarization is an essential characteristic of nerve fibers. The easiest way to prove that point is to measure the resting potential across the membrane of the fiber (see Fig. 22). Such measurements have been made many times by neurophysiologists. They put an electrode at the end of a cut nerve or, in certain dramatic cases, within a nerve fiber, so that it is in contact with the cytoplasm within the fiber. The other electrode goes on the outside of the fiber. The two electrodes are hooked up to a recording galvanometer in much the same way that a voltmeter can be hooked across the terminals of an ordinary battery. In either case a potential is indicated by the number of volts read on the meter. Unlike the battery, the potential across the nerve membrane is very small—of the order of a few thousandths of a volt—but it is nevertheless definitely there. Moreover, it is also clear on the galvanometer that *the outside of the membrane is positive* and *the inside is negative.*

This electrical potential, we know, comes from the arrangement of ions on the two sides of the membrane. Ions are parts of molecules that burst apart, carrying with them electrical charges. Ions, therefore, have chemical properties, as well as the electrical charges that show up on the galvanometer. The whole story of conditions and events at the membrane must include chemical reactions as well as electrical differences. In the next chapter we will deal in more detail with some of the chemical aspects of polarization of nerve membranes, but in this chapter we shall neglect them and stick to electrical phenomena.

Electrical Stimulation. With the concept of polarization in mind, let us turn to the chain of events that gives nerves their enhanced properties of irritability and conduction. These events can be studied by applying electrical stimuli to the membrane of the nerve fiber and then recording the electrical changes that occur. By setting up the right kind of apparatus, physiologists can both stimulate and record with one pair of electrodes put on a nerve. They usually do their experiments with the electrodes on the outside of the nerve but some distance apart. Only in the special case when they want to measure the resting potential due to polarization do they put one electrode 'inside' and the other outside the fiber.

When electrical stimuli are applied through two electrodes on the outside of the fiber, each electrode has a different sign. One is positive and the other is negative, just as are the two electrodes of a battery. The electrode that carries the negative sign is called the *cathode;* the one with a positive sign is the *anode.* The voltage or potential difference between the cathode and anode is the strength of the stimulus.

Electrotonus. So much for the physical situation in stimulating a nerve fiber. Now let us consider what happens (see Fig. 23). When a stimulus is first applied, especially if it is a weak one, it is easy to show that the charge on the nerve membrane changes with the stimulus. At the cathode, the positivity of the outside of the membrane goes down—put another way, the outside of the membrane becomes more negative. This change is exactly what you would expect. It is simply a passive neutralization of the positive ions on the membrane by the negative charges of the cathode. A similar but reverse change occurs at the anode. The membrane at that point becomes more positive, obviously because the so-called 'positive' charges of the anode have added to the positivity of the outside of the membrane. These passive changes in the membrane, directly proportional to the number of charges applied by the stimulus, are called *electrotonus.* The negative change at the cathode is called *catelectrotonus*, and the positive charge at the anode is called *anelectrotonus.*

These electrotonic potentials, as we have said, are passive changes in the fiber of the membrane resulting from the applied electrical potential of the stimulus. It is interesting to note, too, that they spread passively on the membrane. Right under the electrodes the potential is highest, but the potential spreads away from the electrodes much like a pile of sand being poured from a spout. The top of the pile gets higher and higher, but sand rolls down the sides of the pile to make the base of the pile broader and broader. The passive spread of the electronic potential along the membrane is such a central feature of electrotonus that neurophysiologists frequently refer to passive spread of potential on the membrane as electrotonic spread. On this point there will be more later.

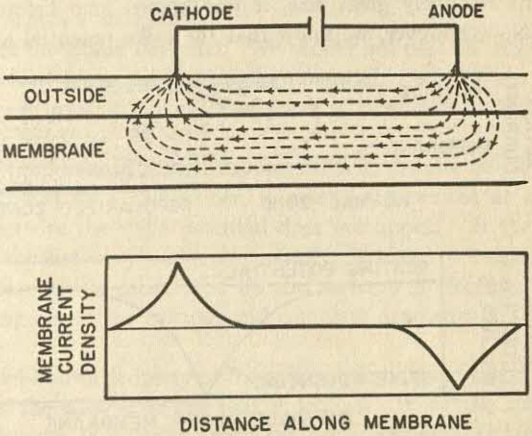

FIG. 23. Diagram of current flow in and along the membrane of a neuron when an electrical stimulus is applied. Currents flow in and along the membrane from the anode to the cathode. There are two foci of current on the membrane, *i.e.*, two peaks of current density. One is at the cathode where currents flow out through the membrane, and the other is at the anode where they flow in.

A word is in order about the flow of current in and around the membrane when an electrotonic potential is applied. We know from elementary electricity that a current will flow whenever a potential (voltage) is applied to a conductor. Although the nerve membrane has some resistance, the resistance is small enough to make the membrane a good conductor. Thus a current will flow. The direction and pattern of the flow are shown in Fig. 23. There you see that current flows out of the membrane into the cathode and from the anode into the membrane. The current flow between the anode and the cathode goes partly along the inside surface of the membrane, partly along the outside surface, and partly within the membrane. The focus of the current flow, however, is through the membrane immediately under each of the two electrodes.

THE ACTION POTENTIAL OF NERVE

Talking about the current flows arising from the electrotonic potential brings us to the action of the nerve itself. The electrotonic effects we have just been describing are passive effects imposed on the nerve fiber by external stimulation. The nerve fiber does not remain passive for long, however, especially if the stimulus is relatively strong. The electrotonic currents disturb the equilibrium of the membrane and set off a set of events in the nerve fiber that is called the action potential.

The Spike Potential. The most explosive and conspicuous event set off in the membrane is the spike potential, familiarly known as the nervous impulse. Because of its relatively great size, it was known long before electrotonic potentials. Now, however, we know that the spike potential arises, at least in normal nervous function, from the electrotonic potential. What happens is this: the outflowing electrotonic currents at the cathode, when they get sufficiently strong, bring about a collapse of the polarization of the membrane. How the collapse occurs is still a mystery—it has something to do with changing resistance or chemical forces maintaining polarization—but it occurs. As a result, the small electrotonic potential leaps very suddenly into a relatively large negative potential, the *spike potential.* If you like, you can think of a leak springing in the membrane at the cathode and all the negative ions, normally kept inside, pouring through the leak to the outside of the membrane.

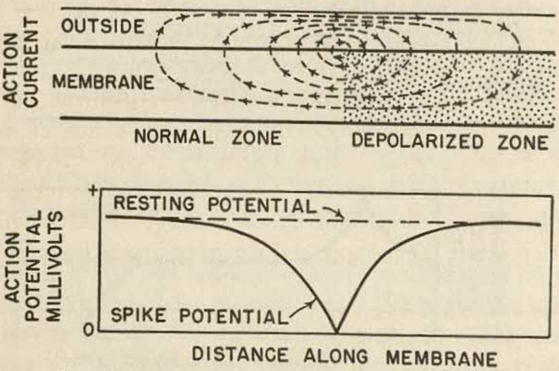

FIG. 24. Diagram of the currents and potentials in and along the membrane of a neuron when a nervous impulse has been started. In the diagram the impulse is moving toward the left. In the forward part of the excited region, currents move out through the membrane. In the back, depolarized region, currents move inward. We ordinarily cannot measure the currents, however, but only record the changes in potential. The spike is a drop of the normally positive resting potential to zero, and it is therefore a negative potential.

The electrical situation in the membrane is depicted in Fig. 24. The electrotonic current moving out through the membrane undermines the membrane and depolarizes it. Instead of the current moving into the cathode, it flows back into the depolarized region of the fiber. Thus, in place of the external circuit previously made with the electrodes, an internal circuit is made in the membrane and its boundary. Currents flowing from the depolarized region inside the membrane move ahead of electrotonic currents to stimulate and break down the membrane ahead. As a consequence the whole disturbance progresses down the membrane. The front of the disturbance is the electrotonic current that depolarizes the membrane, giving a spike potential in the wake of the electrotonic current.

This is just the barest outline of the way in which a spike potential is brought into being in a nerve fiber. There is more to the story, and we shall present more details a little later.

Properties of the Spike Potential. We should not pass on without pointing out the important features of the spike potential. All of them are derived from, or at least implicit in, the description of membrane currents which we have just gone over.

First of the properties of the spike potential is its definite *threshold*. When a stimulus is applied to a nerve fiber, it must be presented at some critical intensity; otherwise the spike potential does not appear. If the intensity is sufficient, it appears very suddenly, usually in about 1 millisecond. The threshold apparently is established by the amount of electrotonic potential needed to bring about the collapse and complete depolarization of the membrane.

A second well-known property of the spike potential, and one closely related to the first, is the *all-or-none law* that it follows. When the spike potential leaps into existence, it is always with the same strength—at least it always goes to the maximum value permitted by the state of polarization of the membrane wherever it takes place. Actually, fibers of different size and in different states of health have spike potentials of different size, but any spike potential appearing at any particular region of a fiber is always as large in size as the membrane at that point will permit; otherwise it does not occur at all.

Thirdly, the spike potential, unlike the electrotonic potential, is a self-propagated disturbance. It moves down the membrane, at a good speed, from the place where it originates. It continues to go along the fiber until it gets to the end, where it dies out. Of course, as we explained above, an electrotonic potential results from the spike potential and moves along the membrane in front of the spike potential. Without the spike potential, however, the electrotonic potential is only a local affair that does not propagate along the fiber.

After-potentials. We have laid great stress on the spike potential because it is the "messenger" that runs along fibers. The complete action potential of a nerve fiber, however, usually includes two more potentials following in the wake of the spike potential (see Fig. 25). For that reason they are called after-potentials.

The first one is a *negative after-potential*, just as the electrotonic and spike potentials are negative in sign. This potential does not appear in some kinds of nerve fibers, and it may not appear in some fibers after they have been fatigued by prolonged or repeated stimulation. The negative after-potential lasts considerably longer than the spike potential; in a typical fiber it may take 15 or 20 msec. to run its course, whereas the spike potential lasts less than 0.5 msec.

The second after-potential is the *positive after-potential.* It is found more universally in nerve fibers. Unlike the negative after-potential, the positive after-potential is enhanced by prolonged stimulation and fatigue. It is even slower in its time course than the other potentials, for in a typical fiber it may last about 80 msec. and under some circumstances it may go on for a second or more.

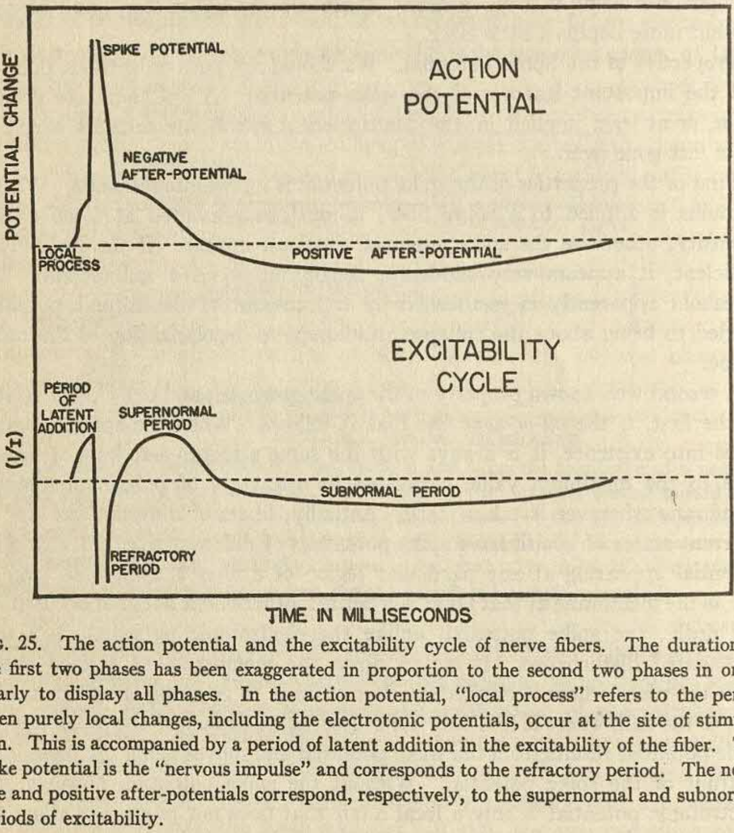

FIG. 25. The action potential and the excitability cycle of nerve fibers. The duration of the first two phases has been exaggerated in proportion to the second two phases in order clearly to display all phases. In the action potential, "local process" refers to the period when purely local changes, including the electrotonic potentials, occur at the site of stimulation. This is accompanied by a period of latent addition in the excitability of the fiber. The spike potential is the "nervous impulse" and corresponds to the refractory period. The negative and positive after-potentials correspond, respectively, to the supernormal and subnormal periods of excitability.

The explanation of the after-potentials is not yet clear. They have a much longer time course than the currents in Figs. 23 and 24. They certainly are some kind of aftermath of the breakdown of the fiber that occurs in the spike potential. Their presence is known to be correlated with the production of heat in the nerve fiber. Thus it looks as though they represent some fundamental metabolic processes connected with the repayment of the energy that the membrane expends in the nervous impulse. More important than explaining them is their relation to changes in the excitability of nerve fibers, which we shall take up in the next section.

EXCITABILITY OF NEURONS

Up to now we have been considering how neurons react with potentials when their membranes are disturbed by some stimulus. There is, however, another important aspect of the reaction of a neuron to a stimulus; it is the question how much stimulus is necessary to produce reactions under various conditions. This is the problem of excitability of neurons.

The Threshold. Because the explosive propagated disturbance that we call the spike potential is an all-or-none potential, and because it is the largest of the potentials measured in a nerve fiber, it becomes a convenient signal for the investigator to use in studying the excitability of neurons. We think of the transition from the electrotonic potential to the spike potential as a *threshold* because it occurs so suddenly and so definitely. The amount of stimulus required to produce the spike potential has thus come to be called the *threshold stimulus*. By measuring the value of the threshold stimulus, under various conditions, we can find out a great deal about the excitability of the neuron and the factors that affect it.

In addition to the term 'threshold stimulus,' there are some other terms that should be defined before we go on. One is *excitability;* this is measured by the strength of stimulus required to produce a spike potential in a neuron. When only a small stimulus is required, excitability is high; when a relatively large stimulus is needed, excitability is low. *Subliminal stimulation* refers to a stimulus producing a local electrotonic response but insufficient in strength to produce the spike potential. Similarly, *subliminal excitation* indicates the arousal of the local response to a point short of the propagated spike potential.

There are some differences among neurons in how their excitability changes with stimulation. They do not all present the same picture. In the typical sensory or motor neuron of the peripheral somatic nerves, however, there usually are four distinct phases of excitability which follow in a sequence after a stimulus has been applied to the neuron. These phases have been called (1) period of latent addition, (2) refractory period, (3) supernormal period, and (4) subnormal period (see Fig. 25).

Period of Latent Addition. This is a very brief period, often not more than 0.5 msec., following the application of a subliminal stimulus, when a second stimulus, if applied, will add to the effects of the first one. It is a period in which the effects of successive stimuli can summate in increasing the local electrotonic potential or, if their combined strength is sufficient, in producing the spike potential. As you might expect, the length of the period of latent addition corresponds to the time that it takes an electrotonic potential to die down.

Refractory Period. Following the period of latent addition, there is typically a short period of depression. If the stimulus that first sets off the local responses is insufficient to produce a spike potential, the depression is only a minor one—stimuli somewhat above normal can still excite the fiber. Then it is called a *postcathodal depression.* If, however, a spike potential has been tripped off by the first stimulus, the depression will be complete. No stimulus, no matter how intense, can arouse a response in the fiber. This complete depression is known as the *absolute refractory period.* Following it there is always a gradual return to normal sensitivity, in which relatively intense stimuli can excite the fiber. This part of the depressed period is called the *relative refractory period.*

It is not possible to say accurately how the refractory period corresponds to the action potential and currents of the nerve fiber, but some general statements are possible (see Fig. 25). The period of latent addition corresponds to the period of the electrotonic potential and also to the area of the membrane in which currents are flowing outward. The spike potential and certainly the absolute refractory period correspond to the part of the action current in which current is flowing inward through the membrane. This is the front part of the area of total depolarization of the membrane. More specifically, the absolute refractory period probably corresponds with the front part of the action potential, while the relative refractory period probably corresponds with the back half, the decreasing phase of the spike potential, when processes of restoration of the membrane must be going on. Neurophysiologists are not willing to commit themselves firmly to this statement because they are unable to make precise measurements of the correspondence (see Lloyd, Lorente de No). Certainly, however, there is a general correspondence of the refractory period and the spike potential.

Supernormal Period. The third phase of excitability following a stimulus is the supernormal period. As its name implies, a weak stimulus, *i.e.*, one less than the normal strength, can excite the neuron in this period of excitability. This period seems to correspond uniformly with the presence of the negative after-potential. The correspondence has been worked out by finding out the times at which both the supernormal period and the negative after-potential occur in particular neurons. Moreover, there are some types of neurons, especially those in the autonomic system, that lack both the negative after-potential and the supernormal period. Both will disappear in almost all nerves when they are subjected to prolonged and intense stimulation or are fatigued in other ways.

Subnormal Period. Finally, ending the sequence of changes in excitability after stimulation, is the subnormal period. This is characteristic of all peripheral nerve fibers whether or not they show a supernormal period. During the subnormal period there is a small but definite reduction in the excitability of the fiber. It takes a larger stimulus than normal to excite the neuron. As you can see in Fig. 25, the subnormal period is the longest of the four phases of the excitability cycle. Moreover, it corresponds with the presence of the positive after-potential in the action potential of the fiber.

SYNAPTIC TRANSMISSION

Until now we have been talking about excitation and conduction in individual nerve fibers. This is only part of the story of physiological functions in the nervous system. It tells what happens in a nerve fiber of a peripheral nerve when a stimulus is applied directly to it. The nervous system, however, is composed of millions of neurons, whose fibers lie side by side in tracts or come together from time to time for conduction from one neuron to another. The next important problem to consider, therefore, is how impulses that have run their course to the end of one neuron initiate impulses in adjacent neurons.

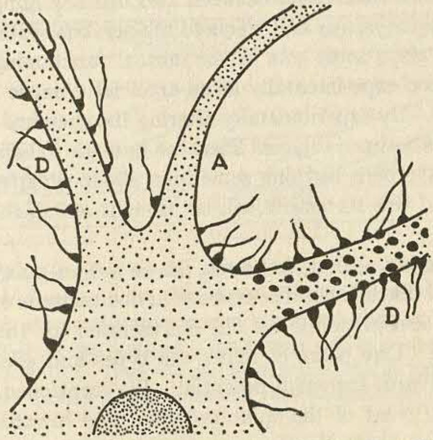

FIG. 26. Part of a ventral horn cell from the rabbit, showing normal synaptic terminals on the lateral surface of its cell body and dendrites *D*, but not on its axon *A* except at the base. Each terminal makes an individual synapse with the ventral horn cell; such synaptic junctions are characteristic of most of the synapses in the central nervous system. (*After Cajal. From J. F. Fulton. Physiology of the nervous system. 2d ed. New York: Oxford,* 1943. *P.* 54. *By permission of the publishers.*)

Synapses. First let us define a few terms and in doing so get a picture of the type of connections neurons make with each other. Neurons, of course, are not directly connected anatomically with one another, for they are individual cells with their own cell membranes. They do, however, interlace with one another to form functional junctures, called *synapses.* The typical synapse in the nervous system has two characteristics of note. (1) The fibers of each axon are divided at the end into many small terminals, which, in turn, often have small bulbous enlargements on them, known as *terminal bulbs* or *boutons* (see Fig. 26). These end upon the dendrites or, in some cases, upon the cell body of another neuron. (2) Each cell usually has many axon collaterals and many dendrites, and these let the neuron make many connections with other neurons, both afferent and efferent. These two characteristics vary somewhat for different neurons and tracts of the nervous system, but they are typical enough to take as the basis for discussion.

Ephapses. There is another type of relation between neurons, which has recently been studied and given the name *ephapse* (see Eccles). This is the functional connection that exists between two neurons lying side by side, as they so often do in the nerves and tracts of the nervous system. The ephaptic relation probably plays some role in the normal functioning of neurons, but it has also been used experimentally as an artificial synapse in the research of neurophysiologists. By experimentally altering the chemical environment of a nerve, the ephapses between adjacent fibers can be made to behave like synapses. In this way we have been learning something about synapses from ephapses. The implications of this statement will be brought out in the subsequent discussion.

Membrane Currents. First, however, let us note a point or two that we have missed so far. Back in the discussion of action currents of peripheral nerve fibers, there were several points we did not mention for the sake of keeping the picture simple. One point concerns the types and effects of membrane currents connected with the spike potential. We mentioned only one current flowing outward in front of the spike potential and inward in the region of total depolarization. Actually there are two internal circuits, not just one, over which current flows. The second current is in the wake of the first. It also flows inward in the region of depolarization but outward in its wake. The whole story is given in Fig. 27.

You have already seen that outward-flowing currents are excitatory and inward-flowing currents are depressing. You have seen that the cathodal electrode is excitatory and the anodal electrode is inhibitory. We can tie these two points together and call outward-flowing excitatory currents *cathodal currents* and inward-flowing currents *anodal currents*. This is a terminology now in common use by neurophysiologists. Applying the terms to the full diagram of the action current in Fig. 27, you will note that the front of the action current is cathodal, the middle of it is anodal, and the tail of it is cathodal again. Thus the currents that flow when a spike potential is propagated follow the sequence cathodal-anodal-cathodal (CAC).

Ephaptic Transmission. The interesting thing about the ephapse is that it can be used to study the separate effects of the currents in the excitation of one nerve fiber by another. By careful dissections of nerve fibers, various sorts of ephapses can be constructed in which one current, two currents, or all these currents can be studied. In Fig. 27 you see a number of different ephaptic situations: some in which two nerve fibers lie side by side and others in which they are adjacent for a short distance and then separate from each other. In each case the lower fiber is made to be 'active' by stimulating it; the upper fiber is the 'resting' fiber. Of course, in this situation what is an outward-flowing current of the 'active' fiber is an inward-flowing current for the 'resting' fiber. Thus, we have to reverse our terms in speaking of the 'resting' fiber. When a spike potential with its associated action current passes along the

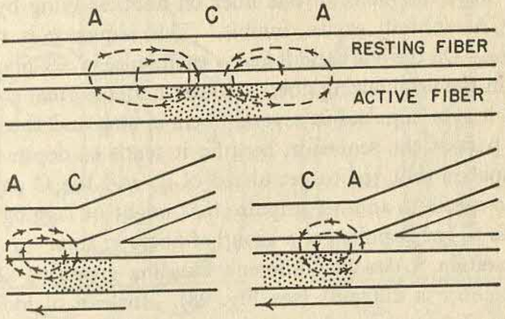

FIG. 27. A schematic diagram of current patterns for neurons in ephases. These are just two of several types of arrangement studied by Arvanitaki in experiments with ephases. The upper diagram is of normal transmission of an impulse along an active neuron (below) while the fiber next to it (above) is resting. The 'resting' neuron is successively inhibited (*A*), excited (*C*) and inhibited (*A*). The lower pair of diagrams is for an impulse approaching and passing a point where another neuron joins and runs alongside the active neuron. (*After Eccles.*)

active fiber, the resting fiber is subjected first to anodal, then to cathodal, and then to anodal currents. And that is the way we shall use the terms. Here are some of the effects that can be demonstrated or surmised from such ephaptic experiments (see Eccles).

1. Anodal currents in the active fiber have a depressing effect on the resting fiber across the ephapse. These are the currents that flow out of the active fiber into the resting fiber—inward-flowing currents, you remember, are depressing.

2. The cathodal currents in the active fiber are excitatory in the resting fiber. They are like the cathode of the electrical stimulus. They can produce an electrotonic potential in the resting fiber. These cathodal currents are outward-flowing in the resting fiber and thus, as we have already seen, are excitatory.

Now, note the sequence of excitation and depression that occurs in the resting fiber as a propagated action potential moves along the active fiber. Any given point on the resting fiber is first subjected to depression by the anodal current of the active fiber, then to excitation by the cathodal current, and finally to another depression by the anodal current that follows. This sequence is important in understanding synchronization in nerves, as we shall see in a later section of the chapter. On the other hand, it indicates plainly that ephaptic arousal of a spike potential is a difficult and rare phenomenon. For the resting fiber no sooner starts to build up a local potential from the cathodal current than it is depressed by the anodal current that follows immediately. Thus the local potential, in ephaptic stimulation, has a poor chance of getting built up to the point where it can trip off the spike potential.

Put another way, the effect of one fiber on another lying by its side is a sequence of ACA—inhibit, excite, inhibit. This sequence is very useful in nerve conduction. On the one hand it keeps an impulse in one fiber from setting off an impulse in the neighboring fiber—at least under normal conditions. On the other hand it gets impulses in several fibers in step and thus synchronizes them. The A part of the sequence, because it tends to depress, slows down neighboring impulses that try to get ahead of it, and the C part, because it excites, tends to speed up another impulse that might be lagging a bit behind. The net result is to get impulses of a group of fibers in step.

Synaptic Excitation. A rather different situation greets us at the synapse because its geometry is different (see Fig. 28). Instead of looking like two cylinders placed side by side, as does the ephapse, the synapse may be regarded as a vertical cylinder placed on a horizontal surface. The vertical cylinder is the small axon terminal of the active neuron; the horizontal surface is the relatively large dendrite or soma of the resting neuron.

As in ephaptic stimulation, an anodal current comes down to the juncture and produces a depressing effect on the resting neuron. Because it has come to the end of the fiber, however, it cannot move on but simply dies away. Immediately following is the strong cathodal current, concentrated in the tip of the axon cylinder. This current can arouse an electrotonic potential in the resting neuron. Again, however, because the current has reached the end of the active neuron, it cannot pass on but dies away. As a consequence, the anodal current that ordinarily follows the cathodal current does not get to the resting fiber—at least not in any great density nor at the cathodal focus of the resting neuron (see Fig. 28). There is, therefore, no depressing effect following the excitatory effect. In brief, the sequence is only AC, not ACA. Thus the resting fiber, now active, has a chance to build up a sizable electrotonic potential.

That, in brief, is the essence of our notions about synaptic and ephaptic excitation. The picture has not yet been checked in every detail, but it is the best synthesis that can be made of a variety of facts now available to neurophysiologists.

Presynaptic Potentials. The spike potential is by far the most conspicuous aspect of the action potential in peripheral nerves. In such nerves, local electrotonic potentials are difficult to detect, and when they are seen, they are only

10 per cent or less of the strength of the spike potential. It is becoming more and more evident, however, that the two potentials are relatively different in size at many of the synapses of the central nervous system. In general, it looks as though local electrotonic potentials are much larger in relation to the spike potential and may even play an important role in the absence of the spike potential. There are many lines of evidence converging on this point, some direct and some indirect. We shall consider them briefly.

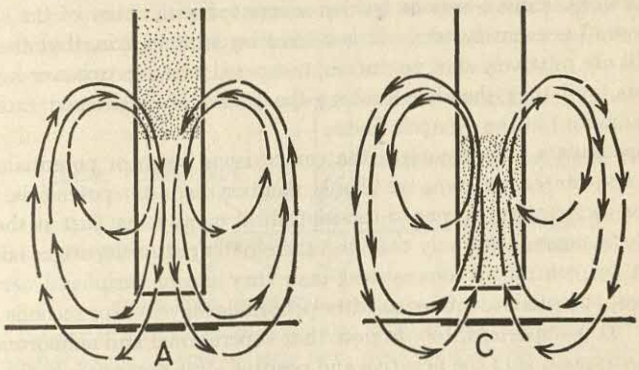

FIG. 28. Diagram of the approach of an impulse to a synapse. The impulse comes down the upright fiber to the relatively large soma (horizontal line) of the next neuron. In the first phase, shown in the left-hand diagram, focal currents flow inward through the membrane of the soma, thus inhibiting it; in the second phase, shown on the right, focal currents flow out through the receiving soma, thus exciting it. The sequence is therefore an anodal effect (*A*) and then a cathodal effect (*C*). (*Slightly modified from J. C. Eccles. An electrical hypothesis of synaptic and neuromuscular transmission, p.* 436. *Ann. N. Y. Acad. Sci.*, 1946, 47, 429–455. *By permission of the New York Academy of Science.*)

In the synaptic terminals of nerve fibers ending on muscle effectors, it can be demonstrated that a smoothly rising and falling potential (end-plate potential) occurs without the abrupt spike seen in the fiber of a nerve (see Eccles). The shape of the potential appears like that of a large local potential. There are technical difficulties of recording with certainty from the presynaptic terminals within the nervous system. It has been supposed, however, that the situation is much the same as it is at muscle end plates; that when the propagated impulse gets to the synaptic terminal, the local potential is enhanced relative to the spike potential. Records made from the vicinity of synapses of certain neurons in the spinal cord show large potentials which resemble local potentials. They may or may not have spike potentials superimposed on them. The reason for enhancement of local potentials in the synaptic region is not clear. It may be simply a matter of the special geometry—shape, size, and position—of the presynaptic terminals and the postsynaptic dendrite or soma; or it may be the result of special electrochemical conditions of the membrane in this region.

Synaptic Potentials. The reason for emphasizing local potentials at the synapse is that such local potentials appear to interact in a special way, giving rise to potentials that have recently been called *synaptic potentials*. The name is assigned because the potentials are not simply those ending in the presynaptic terminal and starting again in the adjacent neuron but depend in some special way on local potentials in both neurons interacting with each other. In any event, there are certainly large local potentials which are not spikes and which do not propagate in all-or-none fashion associated with many of the synapses of the central nervous system. It is interesting to note, too, that these local potentials are relatively slow potentials, compared with electrotonus in peripheral fibers, and they therefore prolong the period of heightened excitability (latent addition) in the synaptic fibers.

After-potentials. To complete the comparisons between potentials in peripheral and central neurons, we should mention the after-potentials. These have been recorded in neurons of the central nervous system just as they have in peripheral nerve. Not only that, but these potentials often are considerably longer in the central nervous system than they are in peripheral nerve. In some cases, potentials identified as after-potentials may last for seconds or even minutes. It is important, too, to note that supernormal and subnormal excitability correspond with the negative and positive after-potentials in the central nervous system just as they do in peripheral nerve. In fact, there are several phenomena of the central nervous system that depend basically on these prolonged periods of supernormality and subnormality.

Synaptic Summation. We have devoted considerable space to explaining synaptic phenomena because they have a number of other consequences for understanding neurophysiological functions (see Lorente de No, Lloyd, Eccles). One of these is synaptic summation. You will notice that in our discussion of synaptic transmission we placed special emphasis on the generation of a local response, not necessarily a spike potential, in the adjacent neuron. For that there is a good reason. In the stimulation of receptors or neurons that are exposed to external stimuli, the intensity of a stimulus usually far exceeds the threshold necessary to set off a propagated spike potential, but when an action potential arrives at a synapse, it is a different story. Action potentials, we have seen earlier, are proportional to the size of the fiber in which they occur. The terminals of neurons at a synapse are not very large. As a consequence, in many cases, if not in the typical case in the nervous system, a single action potential arriving at a synapse is not sufficiently large to produce the complete action potential in the second neuron across the synapse. This kind of phenomenon has been demonstrated rather directly in a number of physiological experiments. All that happens across the synapse is a local response, not a spike potential.

In such situations, nevertheless, spike potentials usually do arise. They do it, however, by the *summation* of two or more local responses (see Fig. 29).

One terminal creates a local process in one area of the second neuron. Another terminal from the same or another neuron creates another sink (local response) across the synapse near the first one. The two local responses spreading a little distance from their focus thus have a chance to summate. The two local responses added together may be sufficient to cross the threshold for the propagated spike potential when one would be insufficient. This kind of summation is called *synaptic summation*. It is considered to be quite typical of synaptic transmission in many regions of the nervous system. In some cases a great many local responses must be summated; in others no such summation may be necessary.

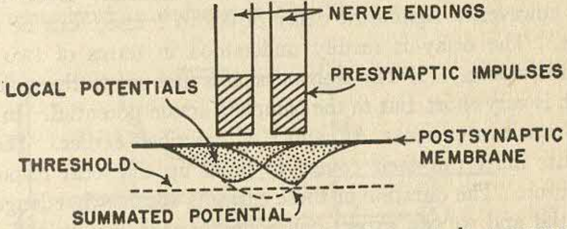

FIG. 29. Diagram of synaptic summation. Two impulses come down nerve endings to the soma of another neuron at about the same time. Each arouses in the soma a local potential that is too small to evoke an impulse. The two local potentials add together, however, to make a potential above the threshold of the neuron. Thus a postsynaptic impulse gets started only through summation at the synapse.

Synaptic summation appears to depend upon two conditions. One is that the summating impulses shall arrive within the period of latent addition; *i.e.*, the local potential generated by one impulse must not have died away before the second impulse arrives or there can be no summation of local potentials. Since the period of latent addition is short, usually less than a half millisecond, this means that impulses must arrive practically simultaneously if they are to summate. The second condition for synaptic summation is that the arriving impulses must stimulate neighboring parts of a neuron. Since the local potentials are really local, two such potentials cannot summate if two impulses arrive at quite disparate points on the neuron. This is apparently a matter of some importance in determining the selection of pathways of conduction in the central nervous system.

Indeed, the mechanism of synaptic summation can be seen indirectly in some of the phenomena of reflex behavior. There are many instances, observed long ago by Sherrington, in which stimulating two different nerves or sets of nerve fibers at the same time will produce a reflex when stimulation of either nerve separately gets no results at all. Looked at from outside the organism, such a phenomenon is *spatial summation*—the summing of two stimuli at different places in the body. We can understand it, however, in terms of synaptic processes if we think of the two different nerves as having terminals on the same somas of neurons in the central nervous system and realize that both sets of terminals must be stimulating the soma simultaneously, thus producing synaptic summation, to arouse an impulse in the soma.

Synaptic Delay. Another consequence of the mechanism of synaptic transmission is synaptic delay. It has been known for a long time that conduction of impulses through the nervous system is significantly slower than conduction along a peripheral nerve. The synapse has been blamed for this delay, and rightly so (Lorente de No). Sometimes the delays are very long—a matter of several milliseconds—but these cases can be assigned to some complex interactions of several neurons, as we shall see a little later. Even under simple conditions, however, a significant delay of 0.5 to 1 msec. can be assigned to the synapse. The delay is readily understood in terms of two aspects of synaptic transmission. (1) The transmission is due not to the spike potential alone, which is very short, but to the complete action potential. In particular, it is due to the two currents, AC and CA, described earlier. The effects of these currents must run their course to build up the local response in the adjacent neuron. The duration of these currents is somewhat longer than the spike potential and we can expect consequently that the synaptic delay will always be slightly longer than the spike potential. Experiments with different spike potentials of varying duration at different points in the nervous system actually demonstrate such a correlation. When the spike potential and action potential are relatively long, so is synaptic delay, and vice versa. (2) The second factor in synaptic delay is the requirement of synaptic summation for initiation of the transynaptic impulse. Where two or more impulses must impinge on a neuron beyond a synapse to produce a transynaptic impulse, there will be some discrepancy in time of arrival of the impulses and this will tend to lengthen the time required to build up a synaptic impulse.

One-way Conduction. There is another basic phenomenon of nervous physiology that can be understood through the arrangement of the synapse. This is one-way conduction at the synapse. If one stimulates a nerve fiber at any point except at its ends, impulses will travel in both directions from the point of stimulation. Across the synapse, however, impulses are conducted in one direction only. To explain such one-way conduction, we now have the fact that transmission at the synapse often, if not always, requires the spatial summation of impulses (McCulloch). Such summation, it appears from anatomical evidence, can occur in one direction and not the other because the dendrites or parts of the cell body upon which axons end are closer together, and thus more capable of summation of local potentials, than are the axon branches that end upon them.

PHENOMENA OF COMPLEX NETWORKS

As you can see by now, we have been progressing in this chapter from the simple to the complex in the arrangement of neurons. We began with events in individual fibers, then moved on to consider excitation and transmission at synapses and ephapses of two neurons. Now, to complete the outline of basic physiological phenomena of the nervous system, we must consider even more complex arrangements of neurons.

Recurrent Nervous Circuits. The myriads of neurons in the central nervous system are arranged in all sorts of ways to carry out many different functions. One of the most important of arrangements is the recurrent nervous circuit (Lorente de No). In this arrangement, nervous impulses set up in one neuron eventually find their way back to the same neuron. In a word, nervous impulses travel in a circle and repeat their paths. Some of the possible arrangements of recurrent circuits are shown in Fig. 30.

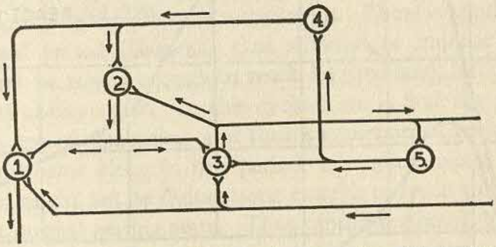

FIG. 30. Diagram of neurons and their synaptic connections illustrating the principle of recurrent (reverberatory) nerve circuits as seen in the IIIrd nerve nucleus. (*After Lorente de No.*)

In the diagram, an impulse comes into the arrangement and can end on both neuron 1 and neuron 3. The impulse that ends on neuron 1 goes out of the system promptly in a simple two-neuron reflex arc. If that were all, the reflex activity would be over in a brief instant. The impulse discharging on neuron 3, however, has its repercussions. Neuron 3 discharges to both neuron 2 and neuron 5. Both these neurons send back fibers to neuron 3. The result is two little reverberatory circuits, one made by neurons 3 and 2 and the other by neurons 3 and 5. Neuron 5, in turn, connects with neuron 4, which goes back again to neuron 2. Thus a three-element circuit is made, involving neurons 3, 5, 4, 2 and back again to 3. All the time, however, neurons 4 and 2 are discharging on neuron 1, the neuron that carries impulses out of the network.

It is easy to see the consequence of this arrangement. Activity once set up in the network can go on for a long time. Instead of the reflex discharge out through neuron 1 occurring once, it will occur over and over again because of impulses coming to neuron 1 out of the reverberatory circuits. Theoretically the reverberation could go on forever—and in some parts of the nervous system it probably does go on as long as the organism lives—but in most cases the reverberation dies down either because the neurons 'fatigue,' becoming more insensitive after prolonged firing, or because their activity is stopped through inhibition (see below). This mechanism of reverberation plays some role in almost all activities of the nervous system from very simple reflexes to complex processes.

After-discharge. The simplest case of such reverberation in observable behavior is the after-discharge seen in simple reflexes. A brief stimulus may be applied to a sensory nerve. The reflex, however, is practically never as brief as the stimulus. The reflex behavior, whatever it may be, goes on for some time after the stimulus has stopped. This has been called after-discharge.

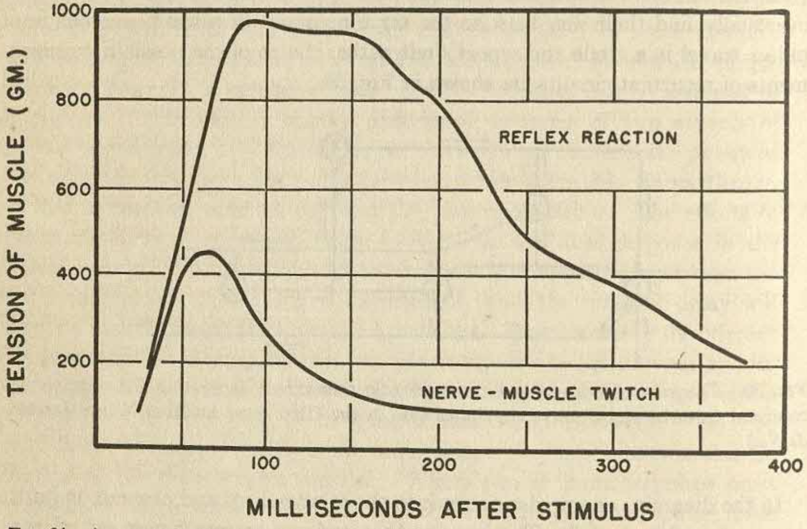

FIG. 31. An example of recruitment and after-discharge in spinal reflexes. The top curve is a reflex of one of the muscles of the cat's leg. The bottom curve is the response of the same muscle to a stimulus applied directly to the motor nerve. The highest tension in the muscle is much greater in the reflex twitch than in the nerve-muscle twitch. It takes the reflex response much longer to subside, too, which indicates that impulses continue to come down to the muscle for some time after the stimulus has stopped—in a word, after-discharge. (*After Sherrington*, 1921.)

It is ascribed to the reverberation of neuron circuits in the central nervous system working as we described them in the illustration above (Fig. 31).

Temporal Summation. There is another phenomenon of simple reflex behavior that is related to the recurrent nervous circuit. This is temporal summation. In some cases of nervous function, one stimulus applied to a sensory nerve does not produce any reflex response. If, however, a second stimulus is applied shortly afterward, say, within 15 msec., a response will occur. Thus the effects of the two stimuli, separated briefly in time, appear to summate. We know that such summation is not a simple summation of local effects at the synapse, because the local potentials that figure in synaptic summation die out in less than a millisecond, whereas temporal summation occurs over many milliseconds. On the contrary, it looks as though reverberatory circuits are behind the phenomenon. The first stimulus, taking Fig. 30 for an example, is unable to discharge neuron 1 but can set up reverberation in the other neurons which subsequently discharge impulses on neuron 1. If at this time a second impulse comes into the network, its effects on neuron 1 can summate synaptically with those from the reverberatory circuits. Thus we can understand temporal summation in terms of reverberation and synaptic summation.

Recruitment. Similar factors account for another familiar phenomenon of behavior. Sometimes, in evoking reflexes, for example, it takes a regularly repeated stimulus, not just a single one, to bring out a response. This is called recruitment. Obviously the kind of reverberating mechanism we have been talking about can help explain such recruitment. There is another factor too—the supernormal period (Gasser). One stimulus or impulse delivered to a neuron may not be strong enough to reach its threshold, but it may set off a subliminal excitability cycle. In this cycle there is first the period of latent addition, then one of depression, and then a supernormal period. If a second stimulus should come along in this period, it might evoke a spike potential even though it might not be quite strong enough to reach threshold when the neuron is in a normal resting state. Thus repeated stimuli, by coming at the right time, may 'recruit' fibers when single stimuli may not.

Inhibition. In closing this very rapid review of the properties of neuron networks, we should deal with phenomena of inhibition. As the term 'inhibition' is used in neurophysiology, it refers to stopping of action of a stimulus rather than starting it. If, in some simple type of reflex behavior, a reflex is set up by one stimulus but can be stopped by another, we speak of the second stimulus as inhibiting the reflex. Or if a stimulus that normally can start a reflex is stopped from doing so by the action of some other stimulus, that too is inhibition.

There are many varieties of inhibition to be seen in nervous functioning. For our purposes, however, it will be sufficient to distinguish two general classes of inhibition, successive inhibition and direct inhibition, and to show how they work.

Successive Inhibition. As the name implies, this refers to the inhibition occurring when two stimuli are used in succession. There are many cases in which a stimulus applied at a certain interval after another stimulus may be ineffective. If, for example, one stimulus follows another by an interval of, say, 20 msec.—*i.e.*, longer than the interval of temporal summation and even of supernormal excitability—its effects are often inhibited. The central synaptic state set up by the first stimulus apparently inhibits synaptic transmission of impulses initiated by the second stimulus.

We can be fairly sure now why this type of inhibition occurs. It is because the neurons in the pathway are in the *subnormal period* of their excitability cycles (Gasser and Graham). The intervals at which successive inhibition occurs is one argument for such an explanation. Another one that is even more convincing is some experimental measurements in which positive after-potentials could be recorded in the spinal cord at the same time as the period of successive inhibition. It is, therefore, fairly safe to say that successive inhibition is not any peculiar property of synapses but rather the effect of the subnormal excitability of neurons.

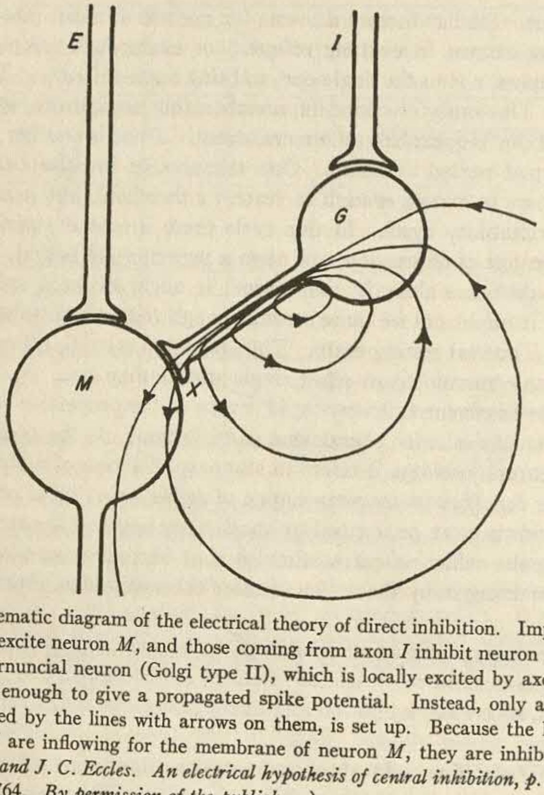

FIG. 32. A schematic diagram of the electrical theory of direct inhibition. Impulses coming in over axon E excite neuron M, and those coming from axon I inhibit neuron M. G stands for a small internuncial neuron (Golgi type II), which is locally excited by axon I but does not get excited enough to give a propagated spike potential. Instead, only a local flow of current, indicated by the lines with arrows on them, is set up. Because the local currents in the region X are inflowing for the membrane of neuron M, they are inhibitory. (*From C. McC. Brooks and J. C. Eccles. An electrical hypothesis of central inhibition, p.* 761. *Nature,* 1947, 159, 760–764. *By permission of the publishers.*)

Direct Inhibition. Perhaps even more common and more important are other cases of inhibition in which two stimuli are applied at the same time and one inhibits the effect of the other. Many theories for explaining this type of inhibition have been put forth from time to time. Even today we have no proof that any of them are right, but there is one which is the most up to date and seems to account for such direct inhibition in the simplest way consistent with all known facts (Brooks and Eccles). It is diagramed in Fig. 32.

In looking at the diagram, keep in mind all that was said earlier about electrotonic potentials and about cathodal and anodal effects. Then make these assumptions: that impulses coming from neuron *E* normally excite *M*, that those from neuron *I* inhibit *M*, and that there is a small neuron *G* interposed between neurons *I* and *M*. It is the short neuron *G* that has the interesting properties. (1) It has such a high threshold that it does not give spike potentials when it is stimulated; it only sets up the local electrotonic potential. (2) It is short enough that when the local potential is set up in it, the inflowing current is at one end and an outflowing current is at the other. You will remember that current flowing out of one fiber inhibits a second resting fiber into which it flows. Thus the final neuron *M* will be presented with a depressing or inhibiting effect from *G*. Since impulses do not propagate in *G*, this is the only effect produced in neuron *M* by neuron *G*.

There is one more step to the story. In talking about synaptic transmission, we noted that a summation of local excitatory effects is usually needed to allow synaptic transmission. Such summation occurs in the local potentials generated at adjacent ends on the soma of neuron *M*. If, however, there are some endings from neurons of the *G* type intervening on the surface of *M*, you can see that inhibitory effects will separate the excitatory effects in *M* needed for summation. Thus even though neuron *E* is exciting neuron *M*, the inhibition will prevent the summation of effects to a threshold level. The result is inhibition of the final neuron *M*.

As we said, this is a hypothetical story. It employs, however, the same concepts that are used in understanding nerve excitation and conduction itself. These concepts fit a vast number of experiments in neurophysiology. There is therefore good reason to put some faith in the theory. The fact of direct inhibition—which is established in many ways—does not, of course, hang on this explanation of it. The theory, however, helps us to get some general insight into the mechanisms of nervous networks and how they are capable of producing both excitatory and inhibitory effects in behavior.

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CHAPTER V

THE INTERNAL ENVIRONMENT

Almost all of the last three chapters has been about the nervous system because this system is the one that has the most to do directly with behavior. The nervous system, however, is only one specialized part of the organism, and there are other cells and organs that also play an important role in behavior. This role is not a direct one—the nervous system is not directly affected—but is exerted through a common medium, the *internal environment*, in which all the cells of the body live. It is the internal environment that is affected by many other tissues and organs of the body. And it is the internal environment that supplies nerve cells with the materials they use and relieves them of their waste products. Thus the internal environment becomes an important physiological factor in behavior. We shall devote this chapter to it.

There are three general aspects of the internal environment that we need to know about. One is the *metabolism of cells*—the biochemical processes that are vital to the existence and life processes of the cells of the body. A second is *intermediary metabolism*—the biochemical events in which food materials are broken down into simple compounds, then recombined in various ways to make the materials from which various cells of the body get the energy for their activities. The third is *homeostasis*—the regulation of the internal environment within the rather narrow limits that are necessary for normal cell functions. These three main aspects of the internal environment—metabolism of cells, intermediary metabolism, and homeostasis—form the main outline of this chapter.

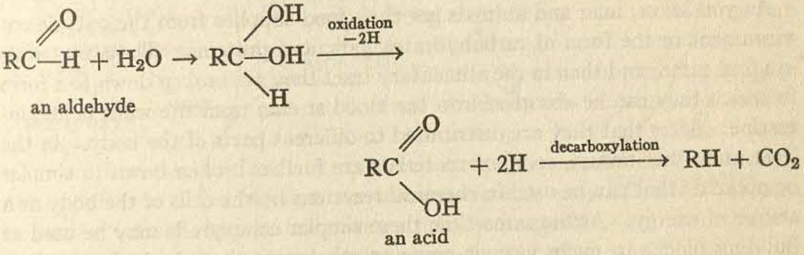
METABOLIC FUNCTIONS OF CELLS

The cell, as you know, is the unit, or building block, of the organism. In this role it not only passes various materials in and out through its membrane but also is the site of many complex chemical reactions. The essential feature of these reactions is the *transformation of energy*, for the cell requires energy for everything it does. Energy is needed for growth, for the storage of foods, and for the repair of cell structures by the synthesis of new materials. It is required, too, for all the specialized functions of cells such as reproduction, secretion, contraction, and conduction. The energy for all these functions comes from chemical reactions within the cell. It therefore is pertinent to look briefly at the major types of chemical reactions that supply this energy.

Oxidation-reduction. One of the most important and best known reactions is the *oxidation* of a compound. There are many types of oxidation, but we can look at all of them as the removal of electrons or hydrogen from the molecule of a chemical compound. Only in certain special oxidation reactions is oxygen actually added to a compound. *Reduction*, conversely, is the transfer of electrons or hydrogen to a compound. Here, for example, is a typical oxidation and reduction reaction involving the compound AH_2:

$$AH_2 \underset{\text{reduction}}{\overset{\text{oxidation}}{\rightleftarrows}} A + 2H$$

Decarboxylation. In the oxidation of certain organic molecules, the product in many cases is a molecule containing a carboxyl group (—COOH). This group happens to be rather low in energy, and for that reason the organism tends to eliminate the group, thereby raising the average energy potential of the remaining carbon atoms. This process of removing carboxyl groups is known as *decarboxylation*. Here is an example of it:



Decarboxylation takes place in the breakdown of chemical compounds. Conversely, when compounds are being synthesized the reverse reaction, *carboxylation*, is of great importance. Probably the most familiar example of this reaction—although not too well understood—is photosynthesis. Light is the source of energy for carboxylation in the photosynthesis of plants, whereas there are other sources of energy when the reaction takes place in animal cells.

Deamination. As you know, protein is one of the major foods that man and other animals eat. The primary building blocks making up protein are the *amino acids*. There are many types of amino acid, but the main feature of them all is an NH_2 group—the amino group. The transferring of this group from one compound to another is one of the ways in which energy is transformed in cells. If, in the transfer, an NH_2 group is lost, it is called *deamination;* conversely, if a compound gains an amino group, the process is known as *amination.* Or in some cases an amino group is transferred from one compound to another; this is *transamination.*

Hydrolysis. There are also many chemical reactions in cells in which water (H_2O) is removed or added to a molecule, thereby aiding the reaction in some way. Probably the most familiar case of this type of reaction is *hydrolysis*, in which water is used to split a molecule into two products. In this case one product receives the H and the other product the OH of the H_2O molecule.

Phosphorylation. The most important of all compounds in energy transformations in cells are the phosphates. In fact, so far as we know at present, phosphates are necessary in some way for all releases of energy in cells. And even more striking is the fact that the energy stored in cells is held there in 'packages,' or units, by organic phosphate compounds. When these complex organic phosphates are broken down, a relatively large amount of heat is set free. Such a breakdown reaction is called *dephosphorylation*. As in all these reactions, there is a reverse process of *phosphorylation*, in which an organic phosphate group is added to a molecule. Also to be noted in passing is the fact that inorganic phosphate is sometimes added to a compound in just the way water is in hydrolysis. Such a reaction is called *phosphorolysis*.

INTERMEDIARY METABOLISM

As you know, man and animals get their food supplies from the outside environment in the form of carbohydrates, fats, and proteins. These materials are first eaten, and then in the alimentary tract they are broken down to a form in which they can be absorbed into the blood stream from the walls of the intestine. After that they are distributed to different parts of the body. In the liver and other tissues, complex materials are further broken down to simpler compounds that can be used in chemical reactions by the cells of the body as a source of energy. At the same time these simpler compounds may be used as building blocks to make various complex substances that the body requires. These processes of breakdown and rebuilding are the major aspects of intermediary metabolism with which we will be concerned.

Dietary Essentials. Although the organism can build up many of the materials that it needs, it must have certain compounds as building blocks to carry on its synthesizing activities. There is consequently a rather large list of dietary essentials without which most higher animals cannot get along. This list includes ten essential amino acids, three indispensable fatty acids, all the vitamins, and certain inorganic elements. Even with all essential materials present in the food, however, an animal cannot function at peak efficiency if the diet is restricted entirely to those essentials. Too much of the animal's energy is spent in building up the complex materials it needs out of the essentials. For the best growth and function some of the so-called nonessential amino acids, as well as a good supply of carbohydrates, must be added to the list of dietary essentials (Rose *et al.*).

The Intermediate Steps of Metabolism. If you consider all the reactions that take place in a typical cell of the body, they seem to be extremely complex. In principle, however, the scheme of intermediary metabolism is relatively straightforward. In the first place, the metabolism of the major food materials takes place in a series of *intermediate steps* in which complex molecules are dismantled section by section or assembled in discrete steps from their

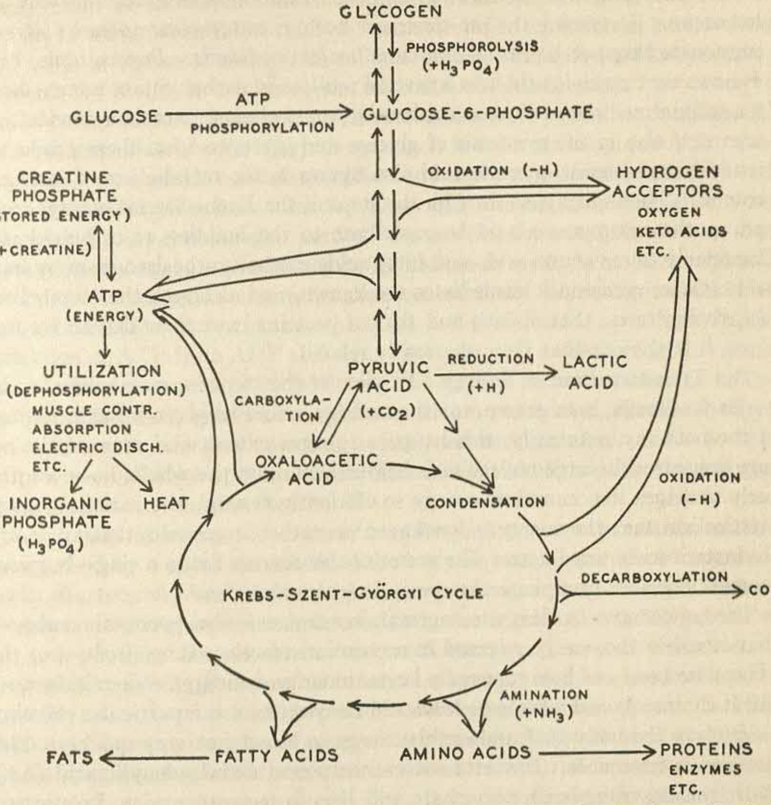


FIG. 33. A schematic representation of carbohydrate metabolism, showing the major steps involved in (1) the breakdown and synthesis of glucose and glycogen, (2) the utilization and storage of energy, and (3) some of the relationships between carbohydrate metabolism and fat and protein metabolism.

elementary components. Second, the reactions involved at each step are all very simple types of the sort described above. As yet we do not know all the details of the various steps and alternative pathways, but we have enough information to form a general idea of what is going on. As an illustration we can take the case of carbohydrate metabolism. We know most about it, and it is of greatest importance in the functioning of the nervous system and thus in the behavior of the organism. In Fig. 33 you can see a diagram of the major steps in intermediary carbohydrate metabolism.

Actually, it is difficult to separate the metabolism of carbohydrates, fats, and proteins. It was known for a long time that the organism could convert one type of material into the others, but the exact mechanism was not clearly understood. Today some headway has been made in understanding these interchanges. It turns out that there are certain intermediate steps that are common to the metabolism of the three major foodstuffs. For example, Fig. 33 shows that pyruvic acid is in a pivotal position in carbohydrate metabolism. It is an intermediate product in the breakdown of glucose to carbon dioxide and water and also in the synthesis of glucose and glycogen from these products. In addition, however, pyruvic acid also figures in the metabolism of fats and proteins. These may pass through the steps of the Krebs-Szent-Györgyi cycle and on through pyruvic acid to contribute to the building of carbohydrate. Conversely, some amino acids and fatty acids can be synthesized from pyruvic acid. Other common intermediates are known, and although the metabolism of carbohydrates, that of fats, and that of proteins have their distinctive features, it is obvious that they are closely related.

The Transformation of Energy. In view of the stepwise metabolism of the major foodstuffs, it might appear that energy would be given up at each step of the pathway. Actually, this happens to some extent, and some of the energy contained in large molecules is lost as heat. On the whole, however, the body manages to accumulate energy so efficiently through the various steps of metabolism that the energy is 'packaged' in rather large units that are ready for instant and varied uses. The secret of this success lies in a single but very unusual chemical grouping—*the energy-rich phosphate bond.*

The bonds between elements or groups in a molecule always contain energy—that is where the energy released in a chemical reaction comes from—but the phosphate bond can hold unusually large amounts of energy. When it does, we call it the *energy-rich phosphate bond.* Moreover, there is a particular chemical reaction in the body that allows this energy to be set free very quickly. This reaction is reversible. It starts with a compound called adenylic acid (AA). With this an energy-rich phosphate will join to form adenosine diphosphate (ADP). Then, finally, the addition of another energy-rich phosphate makes the compound adenosine triphosphate (ATP). These reactions in diagrammatic form look like this:

$$\mathrm{AA} \rightleftarrows \mathrm{ADP} \rightleftarrows \mathrm{ATP}$$

You will note that one molecule of ATP contains two energy-rich bonds. When ruptured, these bonds yield about 12,000 calories per mole of phosphate as compared to the 3,000 calories released from ordinary, energy-poor phosphate bonds. When the terminal phosphate group is removed from ATP it becomes ADP, but ATP can be reformed from ADP through the transfer of energy-rich phosphate bonds to the ADP—just as ATP is formed in the first place.

How do energy-rich phosphate bonds come to get their great energy? To see that, look in the upper left-hand part of Fig. 33. The process starts with glucose—which has been provided from sugar and carbohydrates by the digestive processes. In the first step, glucose reacts with ATP that is already present to form glucose-6-phosphate. Then, reading down and to the left in Fig. 33, you see that this compound is oxidized. In this step energy is set free, but instead of being wasted in heat it is instantly taken up in phosphate bonds. The result is that some energy-rich ATP is formed. That, in a bird's-eye view, is where the energy comes from—the oxidation of carbohydrate.

The energy-rich ATP may either be stored in a more convenient package or be used immediately. One way of storing it is by combining the ATP with creatine (a compound containing amino acids that comes from proteins) in the form of creatine phosphate. In that form ATP can be stored but always be ready for instant release when needed. In muscles, for example, glucose, and more often glycogen, is continually being broken down to form ATP, which is the immediate energy source for muscle contraction. When the muscle is at rest, creatine phosphate stores are built up, and these, too, may be used in the formation of ATP from ADP and AA. There is good evidence that the same sort of cycle is important in producing the energy for such functions as intestinal absorption, calcification of bone, kidney resorption, sperm motility, bioluminescence, electrical discharges, and nervous impulses. Later in this chapter we shall take up some of the biochemical mechanisms involved in the production of the nervous impulse.

Respiratory Quotient. It is sometimes important to get a measure of the energy used by a particular tissue of the body or even of the whole organism itself. Fortunately we know how much oxygen is used and how much carbon dioxide is produced in the complete oxidation of 1 gram of a carbohydrate, a fat, or a protein. We also know how much energy is liberated in each case. From this knowledge it is possible to estimate energy used, *i.e.*, metabolic rate, from the ratio of carbon dioxide production to oxygen consumption. In order to obtain this ratio, known as the *respiratory quotient* (RQ), the tissue or organism in question is placed in a closed system. Into this system measured amounts of oxygen are introduced; from it carbon dioxide is collected and measured. Theoretically the RQ should be about 1.00 when carbohydrate alone is being oxidized, about 0.80 when protein is being oxidized, and 0.70 when fat alone is being oxidized. In actual practice, however, it is impossible to say from a given RQ that the organism is oxidizing a particular substance, for the RQ of the total organism is actually the composite of the RQ's of the different organs and tissues of the body. For example, nerve tissue, which uses carbohydrate almost exclusively, will have an RQ close to 1.00 even when the over-all RQ of the organism is as low as 0.70.

Despite this shortcoming, the RQ has been used widely in physiological and psychological research as an index of the metabolic rate of the organism. When an animal is in a resting state, the RQ is considered a measure of its *basal metabolic rate* (BMR), or the minimum rate at which its metabolic system can release energy. As the conditions of measurement or the state of the organism are changed, the RQ will differ from the BMR. For example, the RQ is influenced by the size, age, sex, and health of the organism, as well as its state of nutrition, activity, the environmental temperature, and a host of other factors. We must hold these factors constant when we use the RQ as a measure of metabolic rate. Furthermore, in interpreting the RQ we must always remember that it is a composite measure of what is going on in all the tissues and organs of the body. It cannot be taken to indicate that any particular one of the major foods is being oxidized.

ENZYMES

How the living organism carries on the many steps in intermediary metabolism in an orderly and rapid fashion was something of a mystery until the discovery of the biological catalysts known as *enzymes*. You may remember from chemistry that catalysts are chemical materials that speed up the rate at which chemical reactions take place yet are not used up in the reactions. Many catalysts are inorganic materials. They need to be present in only minute amounts to do their work. Furthermore, because they do not get used up, they can be used over and over again to catalyze the same reactions. Enzymes in the body have much the same properties as inorganic catalysts, but they are usually complex combinations of protein and other compounds, and they exert their effects in a somewhat more complicated manner than do the inorganic catalysts.

Enzyme Systems. Enzymes often are made up of distinct, but not always separable, parts. For that reason it would be better to call them enzyme systems rather than just enzymes. There is one part of such a system that is known as the *apoenzyme*. This is the protein portion of the system. In the form in which it is found in a cell or in which it is secreted by a cell it may not always show catalytic activity. For that, another part of the system—one having relatively low molecular weight—may be needed. Compounds of this type make up a class called *activators*. In some cases they may be known as *coenzymes* or *prosthetic groups*. Only when such an activator combines with the apoenzyme can we see catalytic properties. Thus it takes both parts to make an enzyme, or enzyme system.

Enzyme Action. While the exact mechanism of enzyme action is not clearly understood in all details, enough is now known to infer a good deal about how enzymes do their work. Figure 34 gives a scheme of the behavior of an enzyme system. In the typical case, the enzyme combines with its *substrate*, the compound whose reaction it catalyzes. Apparently the shape of the complex protein molecules accounts for the very remarkable *specificity* that enzymes show in their ability to direct biochemical reactions in an orderly fashion. Some enzymes appear to catalyze the reactions of only single compounds and then in only one of several possible directions. In such cases, if the structure of the substrate molecule changes even a little, the catalytic effect is lost. This notion, known as the *'lock-and-key theory,'* suggests that the enzyme must 'fit' its substrate in such a way that it strains certain of the bonds of its molecules, thus allowing them to be more readily broken or replaced.

The activity of an enzyme is measured by the amount of chemical change it catalyzes under given conditions. This activity is affected by a number of factors. (1) Within a certain range, the amount of reaction that takes place initially is directly proportional to the *concentration of the enzyme.* (2) With a given amount of enzyme, the initial rate of reaction increases up to a maximum point as the *substrate concentration* is increased, but then no further increase occurs and the rate may fall off somewhat. (3) Most reactions require an *optimal pH*, *i.e.*, an optimal degree of acidity or alkalinity of the medium in which the reaction takes place (see page 103). Different enzyme systems have different optimal pH's, and this optimal pH may vary with such other factors as the temperature, the concentration of salts, etc. (4) Extreme acidity or alkalinity may cause irreversible destruction of enzymes. (5) Enzyme activity also is affected by temperature, and under specified conditions there is usually a specific *optimal temperature.* Up to a certain point the rate of reaction is increased exponentially as the temperature increases, but then the enzyme is

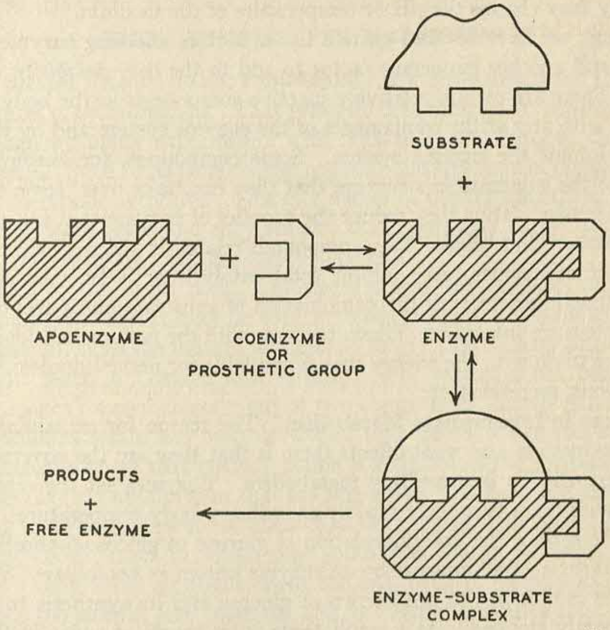


FIG. 34. A schematic representation of the behavior of an enzyme system. (*From W. D. McElroy. The mechanism of inhibition of cellular activity by narcotics, p.* 26. *Quart. Rev. Biol.,* 1947, 22, 25–58. *By permission of the publishers.*)

adversely affected by further temperature increases and the rate falls off. (6) The effectiveness of enzyme action is influenced by such factors as visible light, x-rays, and other types of radiant energy, which may actually destroy or inactivate the enzyme irreversibly. In the normal course of chemical reactions within the organism, many of these factors operate at once. The substrate may get temporarily used up. Or the reaction and other reactions going on simultaneously may change the pH or temperature of the medium.

Although we have covered quite a list of factors affecting enzyme activity, there is still another important factor to add to the list—*inhibition of enzyme action*. There are certain relatively inactive compounds in the body that can compete with any of the components of the enzyme system and by their competition inhibit the enzyme system. Some compounds, for example, are so similar to the substrate in structure that they can 'take over' some of the enzyme molecules. Thus they reduce the supplies of enzyme that are needed for the substrate. In a similar way, compounds related in shape to the prosthetic groups, or coenzymes, may inhibit total catalytic activity. All such compounds that interfere with the combination of substrate and parts of the enzyme system are *inhibitors*. These, together with the factors mentioned above, have a lot to do with the energy that is available for nerve impulses, muscular contractions, secretions, etc.

Enzymes in Intermediate Metabolism. The reason for explaining so fully what enzymes are and what affects them is that they are the governors of almost every step in intermediary metabolism. Enzymes set the rate of reactions and let them take place rapidly at ordinary body temperatures. For example, the rate of the phosphorylation of glucose to glucose-6-phosphate (see Fig. 33) is set in large measure by an enzyme known as *hexokinase*. When this enzyme is inhibited, the breakdown of glucose and its synthesis to glycogen will be partly stopped. As a result there is an excess of sugar in the blood. Similarly, specific enzyme systems are required for many of the processes of oxidation, reduction, amination, etc., which make up the essential links in intermediary metabolism.

All this leads up to another important point about enzymes. *They are pacemakers*. Because metabolism is stepwise, the over-all rate of metabolism can be no faster than the slowest reaction in the metabolic pathway. And because enzyme action is often the limiting factor setting the rate of reactions, the overall rate of metabolism may be paced by a single enzyme. Such an enzyme is a metabolic *pacemaker* (see Hoagland, Crozier). Indeed, experiments tell us that one enzyme in a chain of reactions may become so inhibited that it slows the pace of the entire metabolic cycle. In cases of such metabolic blocks in animals or man, the resulting loss in energy and essential compounds can stunt the individual's growth and even impair mental functions.

Not only do enzymes set the pace of metabolic processes, they may also direct these processes along certain paths rather than along other alternative paths. Enzymes can do this directly because they combine only with rather particular substrates. Thus they favor only certain reactions in which a compound can take part and, as a consequence, discourage other side reactions which, under other circumstances, might take place. For example, of several possible steps pyruvic acid might take at any particular time, such as carboxylation, oxidation, or reduction, an enzyme can favor one and discourage the others.

GENES, ENZYMES, AND METABOLISM

At the present time we do not know exactly how genes determine the hereditary features of an individual. That genes do determine such features is made clear enough by many experiments with mutations and induced changes in specific genes. Such mutations change not only the structure of organisms but also their metabolic activities. This fact makes us believe that there is a very close link between genes and enzymes and that genes may carry many hereditary characteristics by affecting enzyme systems.

In studies of the bread mold, *neurospora crassa,* for example, any one of various mutagenic agents may be used to cause changes in specific genes. In many such mutations the mutant strain is no longer able to carry out a specific biochemical reaction (Beadle and Tatum). For example, the bread mold normally makes its own thiamin out of two components, thiazole and pyrimidine. A mutant strain has been developed that cannot make this synthesis. The biochemists know that enzyme action is required in the synthesis of thiamin; thus they are able to infer that the single gene that has been changed has something to do with presence or absence of the enzyme concerned. There are now many known cases in which gene mutations change enzyme-controlled reactions. They leave no doubt about the link between genes and enzymes. We are not too certain just what the link is. Many scientists are coming to believe that genes are master protein molecules of particular shape that can act as templates for building enzymes of a particular structure (Beadle). At any rate, genes can make for the presence or absence of enzymes or determine the particular structure they have. Then, in turn, the loss of enzymes through gene mutation may block a step in metabolism. Or if their structure is seriously deficient, they may become relatively inactive and slow down metabolic reactions by becoming very slow pacemakers.

All this has more to do with complex functions, including even mental functions, than may meet the eye. Biochemists tell us that the color of flowers, the color of a fly's eye, and the light from luminescent bacteria are all the result of enzyme-catalyzed reactions. Moreover, these complex features of the individual can be changed by gene mutations that bring about changes in enzyme systems, which in turn block the appropriate reactions. Even closer to psychology are examples in man. We shall give just one now. Oxidation of phenylpyruvic acid is a particular step in intermediary metabolism that requires an enzyme. This step can be lacking in certain individuals who possess a certain recessive gene. The result is that people with this defect accumulate phenylpyruvic acid in their bodies and excrete it in their urine. Almost everyone with this defect is feeble-minded! The effect is therefore known as *phenylpyruvic oligophrenia* (see page 533).

You can see from this example that there may be very important links between genes, enzymes, metabolism, and complex behavior. We still have a long way to go and a lot of research to do before we can understand human behavior in terms of these links. In later chapters we shall present more examples of some of them.

VITAMINS

Vitamins are complex chemical compounds that we need for proper growth and other life processes. All that we now know makes us believe that the vitamins are essential parts of the catalytic machinery that paces and directs metabolic reactions. Like enzymes, vitamins are needed in only minute amounts, they do not furnish energy or enter into the end products of most metabolic reactions, and they enter into specific steps in metabolism. In fact, in some cases, experiments leave no doubt that vitamins function just like coenzymes in particular reactions. Unlike enzymes, however, vitamins cannot be put together within the organism but must be present in the diet. Consequently when individual vitamins are excluded from the diet, specific symptoms of deficiency arise, and these can be relieved only by giving the animal the missing vitamin.

The Classification of Vitamins. No good system of classifying vitamins has yet been devised. They are too widely divergent in chemical structure and physiological function, and we do not know enough about the way they act to classify them in terms of their biochemical roles. The best we can do at the present time is to divide the major vitamins into the classic *fat-soluble* (A, D, E, and K) and *water-soluble* (B complex, C, and P) groups and to describe the outstanding deficiency symptoms associated with them. In addition, we can indicate what is known about their physiological function and point out, wherever possible, their role in specific enzyme systems (Table 4).

Antivitamins. Further evidence that vitamins are like coenzymes in an enzyme system comes from recent studies of antivitamins and metabolic antagonists (Woolley). Antivitamins are substances that inhibit the activity of specific vitamins. When an antivitamin is fed to an animal whose diet is complete in all the vitamins and dietary essentials, it will develop symptoms of vitamin deficiency. *Pyrithiamin*, for example, is an antivitamin for *thiamin*, a member of the B complex of vitamins. When less than a milligram of pyrithiamin is added to the diet of mice, symptoms of thiamin deficiency arise faster and in more complete form than they do when the diet is made deficient in thiamin. In this and other similar cases, however, the effects of an anti-

TABLE 4. SUMMARY OF THE MAJOR FACTS ABOUT VITAMINS, INDICATING THEIR MODE OF ACTION AND THE SYMPTOMS OF VITAMIN DEFICIENCY *

Vitamins	Deficiency symptoms	Biochemical and physiological action
Fat-soluble:		
Vitamin A (activated carotinoids)	"Night-blindness"; xerophthalmia, a dry condition and infection around the eyes; growth failure	Plays a role in photochemical processes; is stored in liver; other roles implied but not known
Vitamin D (calciferol or irradiated ergosterol, also irradiated cholesterol)	Rickets, a deficiency in bone calcification, leading to misshapen bones and defective teeth	Facilitates bone calcification and absorption of calcium and phosphorus from intestine; may be important in phosphorylating enzyme systems
Vitamin E	Sterility; degeneration of spermatogenic tissue in male; resorption of fetus in pregnant female	May play role in regulating biological oxidations
Vitamin K	Hemorrhages, due to failure of blood to clot normally	Necessary for production of prothrombin, which is essential for blood clotting
Water-soluble:		
Thiamin (B_1)	Beri-beri in human beings, polyneuritis in animals; both characterized by paralysis starting in hind limbs and slowed heart rate; hyperirritability and convulsions in severe cases	In phosphate form is coenzyme of pyruvate carboxylase, which is required in carbohydrate metabolism for catalysis of pyruvic-acid breakdown; action inhibited by pyrithiamin and related compounds
Riboflavin (B_2)	Skin lesions around the mouth, cataracts, blindness	Prosthetic group for different apoenzymes catalyzing oxidation-reduction reactions; inhibited by isoriboflavin, galactoflavin, and related compounds
Pyridoxin (B_6)	Rat dermatitis; fits in dogs, rats, and pigs	Important in several reactions concerned with amino acid metabolism, transamination and decarboxylation, and other reactions; inhibited by desoxypyridoxine under some conditions

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* After P. H. Mitchell. *A textbook of biochemistry*. New York: McGraw-Hill, 1946. Pp 148–155. By permission of the publishers.

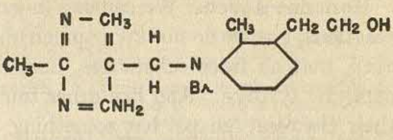
TABLE 4. SUMMARY OF THE MAJOR FACTS ABOUT VITAMINS, INDICATING THEIR MODE OF ACTION AND THE SYMPTOMS OF VITAMIN DEFICIENCY (*Continued*)

Vitamins	Deficiency symptoms	Biochemical and physiological action
Niacin (nicotinic acid and nicotinamide) (B group)	Pellagra, characterized by one or all of the following: dermatitis, gastrointestinal symptoms, and nervous symptoms such as anxiety, confusion, dementia	Required for synthesis of active component of "coenzymes I and II," which function as hydrogen acceptors in some dehydrogenases in biological oxidations; inhibited by 3-acetylpyridine
Pantothenic acid (B group)	Graying of hair and dermatitis in rats	Important in general protein metabolism
Biotin (vitamin H; B group?)	Loss of appetite, muscle aches, and fatigue in man	Concerned in carboxylation reactions
Inositol (B group)	Fatty liver	Unspecified role in fat metabolism
Para-aminobenzoic acid (B group)	Graying of hair in rats	Nature of action undetermined; probably concerned in the synthesis of methionine, purines, and other compounds; sulfanilamide antagonizes its action
Choline (vitamin?) (B group?)	Fatty liver (under some circumstances)	Promotes phospholipid production; aids synthesis of creatine and methionine; important as methyl group donor in metabolism
Vitamin C (ascorbic acid)	Scurvy, hemorrhages of skin and mucous membranes; loss of rigidity of bones and elasticity of muscles	Affects enzymes in vitro; no conclusion on mechanism in vivo; promotes oxygen uptake and hydrogen transfer; inhibited by glucoascorbic acid
Vitamin P (citrin)	Capillary hemorrhages	Closely associated with vitamin C

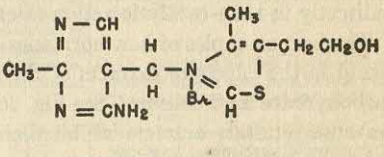
vitamin can usually be overcome by feeding very large amounts, say, thirty or forty times the normal requirement, of the vitamin (Woolley and White).

Antivitamins inhibit vitamins in the same way that inhibitors interfere with enzyme systems. In either case the inhibitor is a relatively inactive molecule which is similar in shape to one part of the enzyme system. In this case the part is the coenzyme, for vitamins seem to behave like coenzymes. For an example of this point look briefly at Fig. 35. There you see that pyrithiamin, an antivitamin, is very similar in chemical structure to the vitamin, thiamin, whose action it inhibits. The difference between them is simply that the sulfur atom in thiamin is replaced in the antivitamin by two CH groups, thus making a benzene ring. It is easy to see why these two compounds can compete with each other in a chemical reaction.

We have used pyrithiamin as an example, but there are many other inhibitors now known. Glucoascorbic acid, by inhibiting certain enzymes, acts as an antivitamin for vitamin C. It will produce symptoms of C deficiency in animals with adequate vitamin C. One of the antivitamins for nicotinic acid, as indicated by deficiency symptoms, is 3-acetylpyridine. Desoxypyridoxine is an inhibitor for pyridoxine in chickens. There are a number of flavin compounds that act as antivitamins for riboflavin in both animals and one-celled organisms. And there are several compounds known to produce the symptoms of vitamin K deficiency. Moreover, there are a host of antagonists not only for the vitamins but for enzyme systems, hormones, drugs, and a number of the dietary essentials. Although many of the antagonists have been studied only in lower organisms, there is good reason to believe that the same basic principles apply just as well to the higher animals.



PYRITHIAMIN



THIAMIN

FIG. 35. Similarity of the structural formulas of thiamin and its inhibitor, pyrithiamin.

HORMONES

Although we know very little about how hormones work in metabolism, we do know how important they are in the physiology and behavior of the organism. We know too that hormones, like vitamins and enzymes, are required in only minute traces by the organism and act as regulators of metabolic activities. Like enzymes, the hormones are made by the organism, but their manufacture is carried on almost exclusively in the specialized cells that make up the various *endocrines*, or glands of internal secretion (Fig. 36). Unlike enzymes, the hormones are not restricted, as most enzymes are, to relatively local effects in the cells that produce them. More typically, hormones are directly

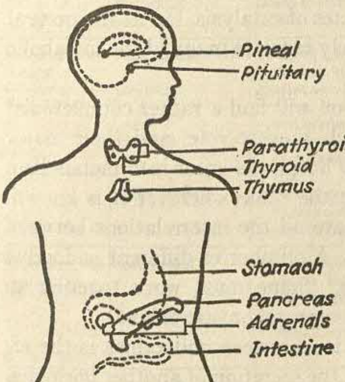


FIG. 36. Silhouette of the human figure showing the location of the endocrine organs. (*Reprinted from Tides of Life by R. G. Hoskins by permission of W. W. Norton & Company, Inc. Copyright 1933 by W. W. Norton & Company, Inc.*)

secreted into the blood stream by the endocrine glands, then they circulate to specialized tissues where they exert their effects on metabolic reactions.

Hormone Action. We can say in general that hormones regulate metabolic reactions, but we do not know much about how they do it. We do know, however, that as trace substances, hormones qualify as possible components of catalytic systems. And like other trace substances—vitamins and enzymes—their chemical 'shape' has something to do with the reactions they control. But there is little direct evidence that any of them act as apoenzymes in enzyme systems. Rather, as well as we can now tell, the hormones, or at least some of them, increase the concentration of particular enzymes, thereby aiding indirectly in their catalytic action (Dempsey).

The best examples of how hormones may work in enzyme catalysis are to be found in the effects of extracts of the anterior pituitary gland and insulin on carbohydrate metabolism. (See Fig. 36 for the names and locations of glands.) Anterior pituitary extracts inhibit the action of the enzyme hexokinase, which is an essential catalyst in the breakdown of glucose. Insulin, in turn, inhibits the effects of the anterior pituitary extracts and thus permits the most rapid catalysis of this important reaction (Price, Cori, and Colowick). Acting together, then, these two hormones are able to regulate accurately the rate of glucose metabolism by controlling the enzyme system required in a crucial metabolic step. Future research may verify the current hypothesis that hormones play an essential role in determining rates of catalysis, but at the present time we can surely say that hormones effectively regulate many of the metabolic reactions of the organism.

Interrelations of Hormones. In Table 5 you will find a rather complete list of the endocrine glands, the hormones which they secrete, and their major functions in the economy of the body. How hormones enter into metabolism interests us, of course, and that is shown in the table wherever it is known. What cannot be given in a table, however, are all the interrelations between hormones. These are many and important. A number of different endocrine secretions have essentially the same effects. Some must work together to achieve an end result; others have reciprocal or antagonistic effects.

Another very important type of interrelation between endocrines is the effect, directly or indirectly, of one hormone on the secretion of another hormone. The best example of this type of interrelation is the *anterior pituitary gland.* This gland puts out a number of hormones, called *tropic hormones,* that stimulate secretion of other glands of the body. For this reason the pituitary gland has often been called the 'master gland.' In a sense it is a master gland, but it is not the sole master of the other glands. Each gland is affected not only by the tropic hormones of the pituitary but also by other chemical factors in the blood. Moreover, many of the glands are controlled in part by nervous impulses coming to them from the nervous system. Thus the interrelationships of glands, of nervous system, and of other metabolic factors are very complex.

TABLE 5. SUMMARY OF THE MAJOR FACTS ABOUT HORMONES, INDICATING THEIR MAJOR FUNCTIONS AND THE ENDOCRINE GLANDS SECRETING THEM

Endocrine	Hormones	Major functions	Comment
Anterior pituitary	Thyrotropic	Stimulates thyroid secretion	Tropic hormone secretion increased by deficiency of thyroid in blood; with hypophysectomy, thyroid atrophies
(Anterior hypophysis)	Adrenocorticotropic	Stimulates secretion of hormones of adrenal cortex	Adrenal cortex markedly reduced in size by hypophysectomy but shows no degeneration
	Lactogenic (prolactin)	Stimulates milk secretion by mammary glands	Liberation of prolactin increased reflexly by sucking stimuli
	Luteinizing (LH)	Required for the development of interstitial cells of testis and ovary and for development of corpus luteum in pregnancy	Male hormone liberated by interstitial cells under LH influence
	Follicle-stimulating (FSH)	Causes development of spermatogenic tissue in male and follicle in female	Ovary stimulated by FSH to elaborate estrogens; in both sexes, both LH and FSH must be present for typical effects of either one
	Growth	Increases bone growth and protein storage	In early life, excess leads to gigantism and deficiency to dwarfism; excess in later life leads to growth of bones in hands and face (acromegaly)
	Diabetogenic	Stimulates conversion of fats and proteins to carbohydrate (gluconeogenesis) and inhibits carbohydrate utilization	Excess leads to hyperglycemia, glycosuria, and ketonuria; deficiency leads to hypoglycemia, especially during fasting
	Pancreatropic	Reduces insulin secretion of pancreas	Repeated injection destroys insulin-producing beta cells of pancreas but also increases growth of islet tissue
	Ketogenic	Leads to formation of ketone bodies	Due to excess fat metabolism; exaggerated in high fat diet and fasting
Posterior pituitary	Antidiuretic	Prevents loss of body water through kidney	In absence, polyuria and polydipsia result if anterior pituitary hormones present
(Posterior hypophysis)	Oxytocin	Excites nonstriated muscles of arteries, intestine, gall bladder, and uterus to contraction	Most marked effect on uterine muscles
	Pitressin	Produces rise in blood pressure by exciting arterial muscles to contract	Little effect on uterine muscles
	Other factors	Induce decrease then increase in oxygen consumption and hyper- then hypoglycemia	Factors not identified, but effects produced by posterior pituitary extract injection
Intermediate pituitary	Intermedin	Expansion of epidermal melanophores making animal darker (fish, amphibia)	Liberation of hormone may be reflexly increased by visual stimulation
	Second factor	Increases basal metabolic rate in thyroidectomized and adrenalectomized animals	Effect produced by injection of extracts
Thyroid	Thyroxine, diiodothyronine, diiodotyrosine, thyroglobulin	Have basic role in tissue metabolism; maintain BMR, utilization of carbohydrate, heart rate; important in growth and metamorphosis	Thyroxine not true hormone, has same effect as extracts. Diiodothyronine and diiodotyrosine less potent and have fewer iodine atoms. Thyroglobulin, found in gland but not in blood, a complex compound containing thyroxine, diiodothyronine, diiodotyrosine, and other compounds. Gland has sympathetic innervation, but denervation does not measurably affect function; inhibited by thiouracil, sulfaguanadine, and other sulfa compounds

TABLE 5. SUMMARY OF THE MAJOR FACTS ABOUT HORMONES, INDICATING THEIR MAJOR FUNCTIONS AND THE ENDOCRINE GLANDS SECRETING THEM (*Continued*)

Endocrine	Hormones	Major functions	Comment
Parathyroid	Parathormone	Maintains calcium and phosphorus balance in blood	In deficiency, tetanus, loss of calcium, rise in phosphorus; not affected by hypophysectomy
Islets of Langerhans (pancreas)	Insulin	Increased conversion of glucose to glycogen and storage in liver and muscles; lowered blood-sugar level; possible increased utilization of sugar	In absence, overproduction of glucose from fat, protein, and glycogen; hyperglycemia and glycosuria, typical diabetic symptoms. Vagal stimulation increases insulin secretion. Inhibited by alloxan, which selectively destroys insulin-producing beta cells of islet tissue
Adrenal cortex	Corticosterone, 11-dehydro-17-hydroxycorticosterone	First two factors serve primarily in increasing carbohydrate metabolism; have slight effect on sodium balance	None of these factors is as potent in all ways as adrenal cortical extract, cortin. The effect on carbohydrate metabolism is by increase in conversion of fat and protein to glucose. In absence of adrenal cortex, food and water intake are reduced, body temperature and metabolic rate drop, pulse slows, salt is lost at kidneys, gluconeogenesis, intestinal glucose absorption, and glycogen deposition are retarded; muscular weakness is general symptom
	Desoxycorticosterone	Primarily increases sodium retention and potassium loss; some effect on carbohydrate metabolism	
	Adrenosterone	Mild androgenic effect	
	Estrone	Potent estrogenic effect	
Adrenal medulla	Epinephrine (adrenalin)	Increased sugar output by liver, increased heart rate, blood vessel constriction, more rapid blood clotting, relaxation of intestinal muscles	Role is primarily in emergency functions, medulla not essential for life; stimulated to secretion through splanchnic nerve
Female gonads	Estrogens (estradiol, estrone, estriol, equilin, stilbestrol derivatives)	Produces estrus and sexual receptivity; female secondary sex characteristics	Elaborated primarily by ovaries, but also by testes, adrenal cortex; found in yeast, petroleum, germinating seeds, palm oil. Estradiol is most potent; estrone, estriol, and others less potent. Calciferol and ergosterol have some effect. Estrogens determine time of onset of puberty in female; excess given to male can delay puberty
	Progesterone	Prepares uterus for implantation and nutrition of embryo	Pregnancy hormone secreted by corpus luteum; action is pronounced only after period of estrogen concentration
	Chorionic (placenta)	Gonadotropic effects similar to LH's	Called *anterior-pituitarylike substance* (APL)
Male gonads	Testosterone, androsterone, dehydroandrosterone	Sexual arousal, secondary sex characteristics	Called the *androgens* (include adrenosterone). Testosterone is most potent; liberated by interstitial cells of testes

These links between the glands, metabolism, and the nervous system pose some serious obstacles for the scientist. His two chief methods of studying hormones in the body are (1) the experimental removal of a gland and (2) the experimental injection or implantation of hormones. The value of either of these methods is limited by the complex linkages in the endocrine system. If, for example, we remove a particular gland, there will be two effects: one will be the direct effect of removal of the hormone that it secretes; the other may be some indirect effects on other glands of the body. We cannot always be sure, then, whether the effects of removing a gland are due solely to the hormone that has been reduced or also to the hormones of other glands affected by the removal. Similarly, if we inject a hormone or implant some glandular tissue, we cannot be sure that this artificial situation actually mimics the normal function of the gland. So, although the methods of gland removal and of hormone replacement have their values in research, results stemming from them must be interpreted with care.

Hormone Inhibitors. Like enzymes and vitamins, the hormones may be inhibited by specific chemical substances. We do not yet fully understand, however, how such hormone inhibitors work. Sometimes the inhibitors damage the cells that make the hormone, sometimes they block the enzyme system needed to make the hormone, and in still other cases they seem to work by blocking the action of a hormone in the metabolic steps in which it is concerned. Some examples of hormone inhibitors of these various types are worth considering briefly.

Alloxan is an inhibitor of insulin, the hormone of the pancreas. Injection of alloxan into an animal is followed by diabetes and all the symptoms of insulin deficiency. If, afterward, a histologist looks at the pancreas of the animal, he can see that alloxan does its deadly work by attacking the beta cells—the specific cells that produce insulin (Goldner and Gomori). Now what is interesting is that hormones of the anterior pituitary gland normally do the same thing as alloxan—at least, repeated large doses of anterior pituitary extract will do it. The effect, however, is not nearly so great and, in the normal individual, does not harm beta cells as much as does alloxan. Nevertheless the pituitary—the master gland—normally masters other glands partly by loosing hormone inhibitors to work on them.

Another somewhat different example of hormone inhibitors concerns the thyroid gland. This gland's secretion can be inhibited by several substances; among them are *thiouracil*, sulfaguanadine, and a number of other sulfa compounds (Astwood *et al.*). In this case, however, no harm to the cells of the thyroid is apparent. The inhibitors seem to work by directly blocking the production of hormone. Thiouracil, regularly administered to an animal, results in all the symptoms of thyroidectomy. Moreover, the thyroid greatly increases in size with only a week of thiouracil administration. This result apparently can be laid at the door of the pituitary, for the inhibition of thyroid secretion seems to stimulate the pituitary to put out more of the thyrotropic hormone that normally steps up activity in the thyroid gland—another nice example of the complex links between glands.

There are still other examples of the third kind of hormone inhibition—direct interference with the effects of hormones. Estradiol and testosterone are two sex hormones that are very much alike chemically. We know that estradiol will inhibit the action of testosterone (Woolley). The explanation of this effect seems to be the same as that for enzyme inhibitors and antivitamins:

because the molecules of the two substances have much the same shape, they compete for the same substrate in metabolic reactions. There are also cases in which impurities in certain hormones repeatedly injected into an animal will develop *antihormones* which fight the action of the hormones. Without going into details, let us simply get the main point, that hormones sometimes compete with each other or with other substances called antihormones.

THE BIOCHEMICAL BASIS OF NERVE ACTIVITY

We have discussed the electrical aspects of nerve activity in some detail in previous chapters. As you know, the activity of nervous tissue depends in part upon changes in the permeability of the membranes of individual nerve cells. When a nervous impulse travels along a nerve fiber, there is a progressive depolarization of the membrane. This is accompanied by changes in electrical potential that may be recorded at any point along the fiber. At the synapse, the electrical changes at the terminals of the first cell may set up depolarization in the second one.

For a long time it was thought that the transmission of impulses across many synapses in the nervous system was not electrical but rather *neurohumoral.* According to this notion, synaptic transmission was achieved by the release at the nerve endings of certain biochemical substances that set up the impulse in the next cell. Nowadays, however, we are quite sure that the activity at the synapse is basically no different from the activity in the nerve fiber. On the other hand, we have become increasingly aware of the biochemical aspects of nerve activity. Biochemical events, we now know, underlie and determine the nerve impulse and its electrical manifestation.

It takes work to build up electrical potentials at cell membranes. Work takes energy, and that means that the metabolic system we have been talking about must furnish the energy for electrical potentials. More specifically, you already know that the action potential of a nerve comes about because the nerve membrane is depolarized, thus destroying a resting potential that was previously built up. The resting potential was set up when the membrane was originally polarized. It is at this point that we must look for the source of energy that can do the work of polarization.

The Acetylcholine Cycle. The energy for this work, many biochemical experiments now suggest, comes from a particular cycle, the acetylcholine cycle (Nachmansohn). This cycle is a part of the general picture of intermediary metabolism discussed early in this chapter (see Fig. 33). Put very briefly and simply, the cycle looks like this:

$$\begin{tikzcd}
\text{acetylcholine} \arrow[d, bend left, "\text{cholinesterase}"] \\
\text{choline and ``acetic acid'' or derivative} \arrow[u, bend left, "\text{choline acetylase and ATP}"]
\end{tikzcd}$$

The key substance is acetylcholine. This breaks down in the presence of an enzyme called *cholinesterase.* The breakdown products can be rebuilt into acetylcholine by the aid of another enzyme, *choline acetylase.* The rebuilding, however, also takes energy, and that energy comes from energy-rich phosphate in adenosine triphosphate (ATP). The ATP, as we have already seen (page 84), can get its energy quickly from the immediate stores in phosphocreatine (see Fig. 33) or somewhat more slowly from the metabolism of glucose and glycogen. That, in brief, is the general picture. Now let us look at it in somewhat more detail.

Cholinesterase. Cholinesterase is an enzyme that acts rather specifically on acetylcholine and a few other substances. For that reason the presence or absence of cholinesterase, as well as some of its chemical effects, is a good indicator of the activity of acetylcholine. Here are some of the things we have learned from the enzyme cholinesterase: In general, the amount of electrical activity in nerves and other tissues is proportional to the concentration of active cholinesterase and therefore, by implication, to the rate of acetylcholine metabolism (Bodansky). For example, the electric organs of certain fish are so constructed that the electrical potential they carry varies continuously from one end to the other. So does the concentration of cholinesterase.

Similarly, we know that the size of the discharge or action potential in electric organs and nerves is cut down in proportion to the degree to which cholinesterase is inactivated by certain biochemical inhibitors. Thus, if *eserine*—which is such an inhibitor—is allowed to penetrate a nerve cell, the amplitude and duration of the action potential will decrease markedly over a 25-min. period. Finally it drops out entirely. The effect of eserine is reversible, however, and the nerve will recover fully and quickly when eserine is eliminated. Another inhibitor, *diisopropyl fluorophosphate* (DFP), may destroy cholinesterase and have an irreversible effect on nerve action if allowed to act over a long enough period of time. There is recovery, however, from mild doses of DFP, and the recovery is clearly seen in the gradual return of normal action potentials.

Choline Acetylase. We know less about choline acetylase, the enzyme responsible for the rebuilding of acetylcholine, than we do about cholinesterase. We do know, though, that it is the agent by which energy stored in phosphate bonds may be transferred to acetylcholine and eventually transformed into the electrical discharges of nervous tissue. To function normally, the enzyme requires not only ATP, which may be formed from phosphocreatine stored in nerves, but also a high concentration of potassium. In addition, it needs an as yet unidentified coenzyme (possibly pantothenic acid) for an activator. It may, however, be partially activated by glutamic acid and other amino acids. On the other hand, choline acetylase may be inhibited by the oxidation products of some of the amino acids. Among such inhibitory products is phenylpyruvic acid, which we know is present in excess in certain types of feeblemindedness.

Site of Action. There is another important point about the acetylcholine cycle that we know something about—where it takes place. The cycle must go on within the nerve cell. For one thing, the application of acetylcholine to a nerve preparation has no effect on action potentials unless it can penetrate into the cell. This it can do at certain nerve endings, but because it is not soluble in fats, it is ineffective when applied to a myelinated nerve fiber. We can go even further. We can say that the events of the acetylcholine cycle take place at the cell membrane. The proof is that axoplasm pushed out of a giant squid fiber contains little or no enzyme cholinesterase, while the great bulk of the enzyme can be found in the remaining envelope (membrane). Hence we believe that acetylcholine metabolism takes place in the membrane, not in the cytoplasm.

Taken together, these facts lend strong support to the hypothesis that acetylcholine metabolism supplies the energy for the action potential of the nerve. Much work remains to be done, but we shall see later that, even in its present form, the acetylcholine theory has been useful in suggesting experiments in physiological psychology. We know that complex function depends upon basic metabolic processes, and any increase in our knowledge of the biochemical basis of nerve function is extremely important in our understanding of complex behavior.

HOMEOSTASIS

The main emphasis so far in this chapter has been on intermediary metabolism, how complex compounds are formed in the body and energy is stored and set free. Much is to be gained by such an approach. It is equally important for our purposes, however, to look at the larger aspects of the internal environment and to see how it is so organized as to provide a favorable medium in which the various cells of the body can carry out their normal duties.

The Concept of Homeostasis. What all cells must have is a favorable equilibrium between them and their environment. On the one hand most of the metabolic reactions that occur in the cells demand a constant supply of materials. On the other hand these reactions themselves produce variations in the temperature, pH, osmotic pressure, etc., of the internal medium that would be detrimental to cell function unless checked or counteracted. Most cells of the body, however, lost some of their ability to maintain equilibrium with the environment when they differentiated to perform special functions. As a consequence, few cells can maintain a favorable internal equilibrium all by themselves. They have had to collaborate and to some extent specialize to see that their environment is maintained relatively constant under a wide variety of conditions.

Physiologists use the term *homeostasis* to refer to this constancy of the internal environment or, more strictly speaking, the maintenance of the internal environment within the rather narrow limits conducive to normal cell function

(Cannon). Their studies tell us that the typical warm-blooded animal maintains a constant body temperature, pH, blood pressure and heart rate, blood-sugar level, salt and water balance, calcium and phosphorus balance, etc. Indeed, the number of factors that are relatively constant in the body is remarkable.

There are several different but interrelated factors in this homeostatic equilibrium. The hormones are one. There is a long list of others: the lungs, through which carbon dioxide is excreted and oxygen taken in; the circulatory system, which controls the distribution of blood to the various tissues; the kidneys, through which various products of metabolism, particularly those from the breakdown of proteins, are excreted; the digestive tract, by means of which essential materials are brought into the body; and finally, the nervous system, which takes part, directly or indirectly, in regulating the other homeostatic mechanisms. Of particular importance to us are the mechanisms that regulate blood-sugar level, hydrogen-ion concentration, and oxygen supply, for the functioning of the nervous system, and thus behavior, crucially depends on their being kept uniform within very narrow limits of variation.

Blood-sugar Level. In most mammals, the concentration of sugar (glucose) in the blood stays between 60 and 90 mg. per 100 cc. of whole blood. *Hypoglycemia*, or depression of the blood sugar below this lower limit, deprives the cells of the carbohydrate they need, because the rate at which glucose can get into cells depends in part on how much is in the blood stream. Most tissues of the body can function adequately for fairly long periods of time at low blood-sugar levels, but the nervous system is especially dependent upon steady supplies of glucose. It can store very little carbohydrate, and it cannot readily make use of other materials for its metabolic functions. As a result, when an animal has hypoglycemia it will go into a coma and die if something is not done about it.

The converse situation, *hyperglycemia*, *i.e.*, elevation of blood sugar above the upper limit of normal concentration, has a less dramatic effect on the nervous system and cell functions in general. Nevertheless, prolonged and severe hyperglycemia can lead to widespread metabolic derangements. When the blood sugar reaches about 160 mg. per 100 cc., the excess sugar is excreted in the urine, and along with it go large quantities of water and other organic and inorganic constituents of the blood plasma that are essential to life. Prolonged hyperglycemia can lead to all the symptoms of the disease, diabetes.

Function of the Liver. A central factor in keeping blood sugar at the right level is the activity of the liver (Fig. 37). In the first place, the liver can store fairly large amounts of carbohydrate in the form of glycogen. Secondly, under appropriate stimulation it can either convert glycogen and secrete it into the blood in the form of glucose or it can remove glucose from the blood and store it as glycogen. Both these activities depend on specific endocrine influences and on how much carbohydrate is available to the liver. With normal food intake, most of the glycogen in the liver comes from carbohydrate absorbed through the intestine.

But the liver can also convert fats and proteins into carbohydrate—a process called *gluconeogenesis*. The rate at which gluconeogenesis can take place is in-

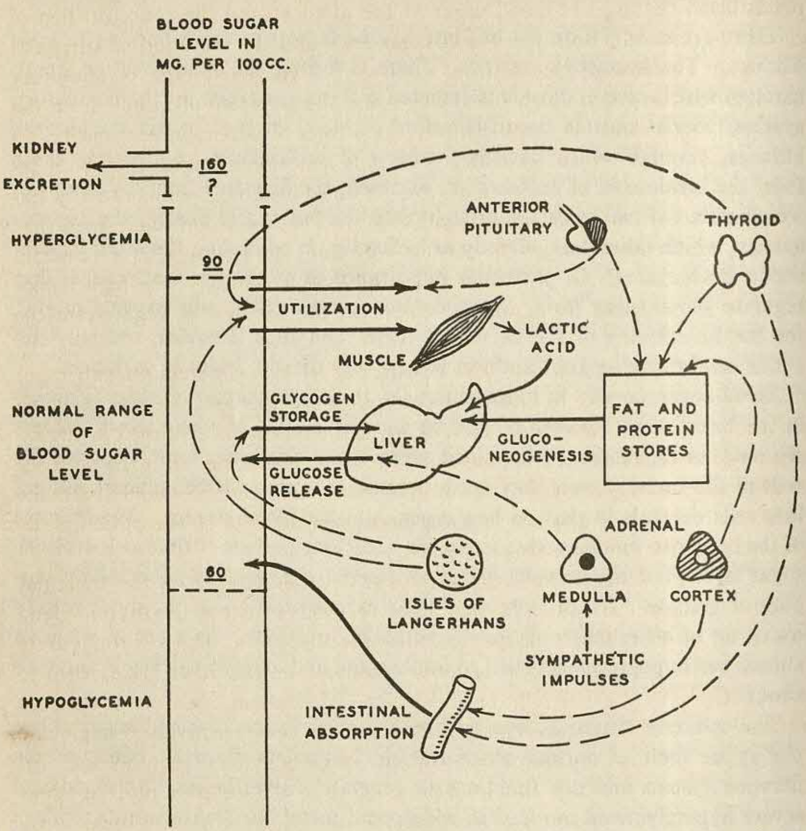


FIG. 37. A schematic representation of some of the factors influencing blood-sugar level. Solid arrows indicate carbohydrate transport, absorption, utilization, formation, and excretion. Broken arrows show factors that influence these processes and thus the blood-sugar level. (*After M. Bodansky. Introduction to physiological chemistry. 4th ed. New York: Wiley,* 1938. *P.* 318. *By permission of the publishers.*)

creased by the hormones of the adrenal cortex, the anterior pituitary, and the thyroid gland. When the organism is fasting, absence of any one of these hormones, particularly of the anterior pituitary hormones, will bring about marked hypoglycemia, because the only remaining way of getting carbohydrate is gluconeogenesis and that too has been reduced to a minimum. With a normal endocrine balance, on the other hand, fasting has no great effect on blood sugar, because the liver can keep pace with the demand for carbohydrate through the conversion of fats and proteins.

Whether the liver will secrete glucose into the blood or tend to remove it depends upon the level of blood sugar at the moment and the concentration of certain hormones. Both low blood-sugar level and the secretion of adrenalin will cause a release of glucose from the liver. Glycogen storage, on the other hand, is encouraged by high blood sugar and the secretion of insulin from the isles of Langerhans. As you can see, the effects of adrenalin and insulin on blood-sugar level are antagonistic. But it is also worth noting that both insulin and adrenalin produce conditions in the blood that will normally encourage a return to blood-sugar equilibrium. The low blood-sugar level that follows insulin injection or its natural secretion, for example, is a powerful stimulus for the release of glucose from the liver. Similarly, the high blood-sugar level produced by adrenalin stimulates the removal of sugar from the blood.

Utilization of Carbohydrate. Blood-sugar level also depends on two other major factors: the rate of intestinal absorption of sugar and the rate at which the tissues use carbohydrate. How much carbohydrate is absorbed in the intestine depends, of course, on how much the animal is eating. But the presence or absence of the hormones of the adrenal cortex and thyroid gland also make a difference. In the absence of these hormones the rate of absorption is decreased; in their presence it is increased.

The rate at which carbohydrate is used depends largely on the muscular activity of the animal. In addition, however, the hormone of the thyroid gland can speed up metabolic processes and increase the rate at which carbohydrate is used. The hormones of the anterior pituitary, on the other hand, seem to depress the rate of carbohydrate utilization. The reason, it seems, is that the anterior pituitary hormones can inhibit one of the enzymes involved in glucose breakdown. Thus they slow down the rate of carbohydrate metabolism. Insulin is believed to offset this inhibitory effect of the anterior pituitary hormones; at any rate it seems to increase the rate of carbohydrate breakdown. Moreover, it increases the rate at which blood sugar, at a given concentration, gets into the cells of the body where it can be used.

Hydrogen-ion Concentration. As you know, many of the metabolic reactions that take place in the body produce relatively strong acids and bases. The dissociation of acids and bases in water gives rise to hydrogen ions ($H+$) and hydroxyl ions ($OH-$) respectively, and an excess of one or the other will make the medium acidic or alkaline. It is customary to refer to the acidity or alkalinity of a medium in terms of its hydrogen-ion concentration, or pH. The values of pH are designated in a logarithmic scale in which low values represent acidity and high values alkalinity. The neutral point on this scale is 7.0, and it is interesting to note that the normal pH of the blood is about 7.4, *i.e.*, slightly alkaline. The extreme limits of variation of the pH of the blood are 7.8 to 6.8. Above or below these values, cell functions, particularly those of the nervous system, are so disturbed that death results. Thus it is essential that the hydrogen-ion concentration of the internal environment remain stable.

The body has three ways of keeping the pH stable. One is a set of *buffers* in the blood. These are chemical materials that can 'bind,' or take up, acid ions. There are usually plenty of buffers in the blood to catch, at least temporarily, the acids coming into it from the metabolism of tissues. A second way of keeping the pH stable is by the excretion of acids from the kidneys. This works particularly for the acids that are products of protein metabolism. Such acids are buffered temporarily in the blood, then excreted by the kidneys. Finally, there are the lungs, through which carbon dioxide escapes. Carbon dioxide in solution is acidic, and it is the ultimate product of carbohydrate metabolism. It gets out of the body through the lungs.

There is a little more to say on this last point. If carbonic acid in the blood gets too high, there are two ways of speeding its escape through the lungs. One is by increasing the rate of breathing. The other is by increasing the circulation of blood through the lungs. There are neural mechanisms for doing both these things. In one case carbonic acid in the blood excites the 'breathing center' in the hind part of the brain to speed up breathing. In the other carbon dioxide in the blood excites vasomotor centers so that blood vessels are constricted, blood pressure is increased, and blood courses more rapidly through the arterioles of the lungs. This is a good example of the interrelation between the nervous system and the internal environment to keep the latter as constant as possible.

Oxygen. This, of course, is needed directly or indirectly for the oxidation reactions in intermediary metabolism. All needed oxygen must get into the body through the lungs. There it is absorbed into the blood through arterioles, where it combines immediately with the hemoglobin of the red corpuscles. When the amount of oxygen in the air is normal and when breathing is also normal, the red corpuscles absorb about 95 per cent of the oxygen they could possibly carry. If, however, the oxygen coming in through the lungs is less than it should be, the oxygen saturation of the blood is cut down—a condition called *anoxemia.*

It is easy to infer from this discussion that oxygen is carried from the lungs to the tissues by the red corpuscles. This transport must go on at a normal rate or there are dire results. A balance in oxygen transport is held, it is interesting to note, not by any direct reactions to oxygen deficiency, but rather by the pH of the blood, especially the pH changes that come about from too much carbon dioxide or lactic acid. When, for some reason, the tissues need more oxygen than they are getting, the acidity of the blood steps up the oxygen supply in one of three ways: (1) As we have just seen, acidity increases the breathing rate, thereby bringing oxygen into the lungs more rapidly. (2) Also as we have just said, the circulation of the blood through the lungs is stepped up. (3) Finally, there is a special response of the blood vessels of the needy tissues to too much acidity. They expand so that more blood will get to the tissues.

As you can see, there is a common method for keeping both the pH and the oxygen supply on an even keel in the internal environment. This single mechanism for regulating the two factors works because an excess of carbon dioxide and a deficiency of oxygen usually go along together in the body's metabolism. Breathing increases oxygen supplies and decreases carbon dioxide in the blood. Similarly, an increase in blood supply to the tissues carries away more carbon dioxide and brings up more oxygen. That is why pH generally and carbon dioxide specifically can serve to regulate both carbon dioxide and oxygen supply.

Regulatory Behavior. So far, we have talked only of relatively automatic physiological mechanisms that maintain the constancy of the internal environment. As you will see in later chapters, the behavior of the organism can also contribute to homeostasis. In such cases we refer to the behavior as regulatory behavior, for it is initiated by some adverse condition of the internal environment and it serves to bring about beneficial physiological changes. We cannot go into details at this point, but one illustration will serve to show what we mean.

As you know, birds and mammals must maintain their body temperature within very narrow limits. If the temperature outside a warm-blooded animal gets cold, a number of things take place to keep the animal's body at the same temperature. In the first place, the rate of heat production in the body will increase. This comes about through stepped-up thyroid function, which improves the general metabolic rate through quickened heart rate and heightened muscular activity. In addition, the animal may increase its heat production by shivering. Secondly, changes will take place that reduce the rate of heat loss from the body. The superficial blood vessels will constrict; the hair of the body will erect, forming a good insulating coat in the case of certain furry animals; and the animal may roll into a ball, exposing only a minimum of body surface. At the same time the animal may behave in such a way as to reduce the heat loss and increase heat production. If possible, it will move to a warmer area of the environment. Given access to building materials and a variety of foods, it will build a nest, hoard large stores of food, increase its food intake, and select a diet of high caloric value.

A great deal is known about behavior of this sort, and we shall have more to say about it later. The important thing to remember here is that the coordinated activity of the nervous system is an important factor in keeping the internal environment constant.

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CHAPTER VI

THE CHEMICAL SENSES

There is very little that we really know about the chemical senses. In fact, probably no other senses are so poorly understood. This sad state of affairs, however, is not anybody's fault. Investigators have tried hard enough. They have carried out hundreds of experiments and given us dozens of theories. The trouble seems to center partly in the nature of the stimulus and partly in the complex and relatively inaccessible structures of the chemoreceptor system.

Chemical Stimuli. The stimuli, of course, are chemical substances. Modern chemistry tells us pretty well what the structure and properties of the stimuli are. Unfortunately, every chemical substance, no matter how simple or complex, has a good many different properties, and we are unable to figure out just which properties are significant in stimulating the chemical receptors. There is trouble, too, in applying chemical stimuli to the receptors under controlled conditions. The smell receptors are located in a remote recess of the nasal cavities, and it is difficult to know what proportion of an odorous gas reaches and affects the smell receptors. The taste receptors are in nooks and crannies of the mouth's surface. It is hard to make sure that liquid and solid stimuli actually get to them and, when they do, to make certain that they are washed away when we want to apply a second taste stimulus.

Neural Centers and Pathways. More troubles face us in the central nervous system. The olfactory centers and pathways, for the most part, lie on the ventral surface of the brain facing the floor of the cranium. This region is difficult to work in with either surgical or electrophysiological procedures. The olfactory system, moreover, is massive and complex, as far as we can tell from its gross anatomy. The taste centers and pathways, although not so complex, are all mixed up with the cutaneous system. This makes them difficult to study.

Because of these limitations on our present knowledge of the chemical senses, it seems best not to take you into all the details of the theories and experiments that have been put forth in the field. They would probably only confuse you and not increase your understanding of the physiological mechanisms. Instead we are going to make this a brief chapter that concentrates on the few most important facts and experiments about the chemical senses and gives you only the gist of the more theoretical and less established aspects of the field.

The Chemical Receptors. Not just two but rather three classes of chemical receptors are to be distinguished in all vertebrates: the olfactory, the common chemical, and the gustatory receptors. They are all more sensitive to chemical stimuli than to other kinds of stimuli. It appears, moreover, that the chemical stimuli for all of them must be in solution to be effective. To be sure, odors are in gaseous form before they arrive at the olfactory receptors, but once there, they enter into solution with the mucous materials bathing the olfactory receptors. Thus for the receptor itself, the olfactory stimulus is like the others—a solution.

There are, however, differences in the types of chemical stimuli to which the three classes of receptors are sensitive. The chemistry of these differences is complex. One general distinction is that the stimuli for olfaction must exist in gaseous form at ordinary temperatures in order to make their way to the receptors, whereas the stimuli for taste must be soluble in water and other fluids. A second point is that the chemical sensitivities of the different classes of receptors are different, for stimuli that we know reach the receptors may excite one type and not the other. Finally, we may note that the smell receptors are, in general, more sensitive than the taste receptors. These, in turn, are more excitable than the common chemical receptors.

Of importance, too, are the structural differences in the three classes of sense organs (Parker). We used these differences earlier to illustrate the different directions in which differentiation may proceed in the development of receptors (see Fig. 3). The most primitive is the common chemical receptor. It consists simply of a neuron with frayed endings which encircle comparatively undifferentiated epithelial cells. The gustatory receptor, on the other hand, is made up of a neuron (the 'primary sense cell') and a highly differentiated epithelial cell (a 'secondary sense cell') upon which the neuron ends. The olfactory receptors, however, have no differentiated epithelial cells. The neuron itself has migrated to the periphery—although not close enough to suit the research worker—and has been fashioned into an extremely sensitive receptor mechanism by the elaboration of many hairlike elements. Such structural differences in the three classes of receptors, as we have already noted (page 16), are representative of trends that have been observed in the differentiation of receptors in general.

COMMON CHEMICAL RECEPTION

There is so little to say specifically about the common chemical receptor that we might as well say it and be done with it (see Crozier). The common chemical receptors are more widely distributed in the body than the other chemical receptors. The chief problem, in fact, is to distinguish them from the receptors for pressure and pain, which are also liberally distributed throughout the skin.

Receptors. Free nerve endings associated with epithelial cells can subserve either pain or pressure or common chemical reception. But even though one cannot tell the difference with the naked eye, it is possible to show that common chemical receptors are different from the other two (Crozier, Moncrieff). With cocaine one can anesthetize the touch and pain receptors, but after sensitivity to touch and pain are gone, the application of an acid—a stimulus for the common chemical receptor—can still be felt. Conversely, after the common chemical receptors have become adapted to stimulation by acids, one can feel pressure or pain.

Neural Pathways. Common chemical receptors are widely distributed throughout the body, especially in exposed moist surfaces such as those of the mouth and throat. They are served by fibers from various cranial and spinal nerves, but they do not seem to be represented in the central nervous system by any special pathways or centers. They seem to run along with the fibers for taste or the skin senses. More research, however, is needed on this point.

Appropriate Stimuli. The most effective stimuli for the common chemical receptors are dilute solutions of acids, alkalis, and salts, or, in general, any substances that ionize well or tend to dehydrate tissues. The threshold concentration of hydrochloric acid and of sodium hydroxide, for example, is about .01 normal (.01*N*). (A normal solution is one in which 1 mole of a substance divided by the valence of the ions into which it dissociates is dissolved in 1 liter of water. A mole is the molecular weight of a substance in grams.) The threshold for alcohol, which is relatively nonionizable, is about 3*N*. Compared with the thresholds of taste or smell these are very high; this fact reflects the relatively primitive nature of the common chemical receptors.

OLFACTION

In this summary of the little that we know about the physiological mechanisms of smell, we shall proceed in logical order from the stimulus to the brain. First we shall consider the problem of sensory qualities and their relation to olfactory stimuli, then the olfactory receptor mechanism, and finally the structure and function of olfactory centers and pathways.

Theories of Olfactory Quality. There have been countless theories of the qualities of smell sensations and of how they are related to properties of olfactory stimuli (Moncrieff). Most of the theories, and certainly all the prominent ones, assume that the kind of odor we sense depends upon which receptors of the olfactory membrane are stimulated. The theories differ mainly on the number of qualities that are considered to be primary and on the properties of odors that are assumed to be related to the quality.

Two of the most widely publicized theories assume a small but definite number of olfactory qualities. Zwaardemaker, one of the early workers in the field, who contributed more to our facts about smell than to theory, proposed nine olfactory qualities. He named them ethereal, aromatic, balsamic, ambrosial, alliaceous, empyreumatic, caprilic, repulsive, and nauseating. These names probably are of little value today, but they indicate the kind of fundamental olfactory qualities that Zwaardemaker proposed. Another somewhat more popular theory is that of Henning, calling for only six basic qualities: spicy, flowery, fruity, resinous, burnt, and foul. Another theory postulates only four basic qualities (Crocker and Henderson). And there are many other theories in which an attempt is made to classify odors in a small number of categories. None of these theories has proved very satisfactory. In every case there are phenomena that make the theory at best a rough approximation. Indeed, at present we have no theory good enough to warrant much attention from a physiological point of view.

Theories of Stimulus Properties. Closely related to the question of smell quality is the problem of what properties of olfactory stimuli are effective in exciting the olfactory receptors. On this point there are two general classes of theories, chemical and vibrational. Chemical theories are the ones that have been most widely held. They assume that excitation of the olfactory receptors is due to complex biochemical reactions in which the stimulus reacts with substances in the receptors to arouse impulses. These theories have led to a great deal of experimental work on the kinds of chemical substances that smell and on what kinds of smells they excite (see Moncrieff). This work has been of great practical benefit in perfumery and sanitary engineering. These theories also have been expanded to include notions of the kinds of chemical groupings and structures that give rise to different smell qualities. Here they have not been very successful, for it is not yet possible to make any simple set of statements about chemical structure and excitability or smell quality.

Not so well known but also the subject of a good deal of experimental work are vibrational theories of smell. In these theories it is assumed that the molecular activity of the odors rather than their molecular structure determines excitation and smell sensation. The way in which we ordinarily study molecular activity is to see what bands of light are absorbed or deflected by a chemical substance. If, for example, a substance strongly absorbs light of a given frequency or wave length (see page 148), it indicates that there are intramolecular vibrations of the substance of the same wave length. By such methods, different investigators have secured evidence leading to three different vibrational theories of olfactory stimulation.

One theory, the infrared theory, is a very old one but has recently been revived (Beck and Miles). This theory holds that the absorption of the invisible infrared rays is a property important in excitation. The body, being heated, does indeed emit infrared radiation, and it would be possible for the olfactory receptors in some way to be sensitive to the infrared-absorbing properties of olfactory stimuli. It is also true, as discovered many years ago, that a great many gases that have odors also have absorption bands in the infrared. The only trouble is that there are some substances which smell but which have no infrared absorption, *e.g.*, paraffin and carbon disulfide. And there are others, such as carbon dioxide and water vapor, which have infrared absorption but do not smell. Unless some new and very convincing evidence is forthcoming, it is doubtful whether there is anything in such a theory (see Moncrieff, page 287).

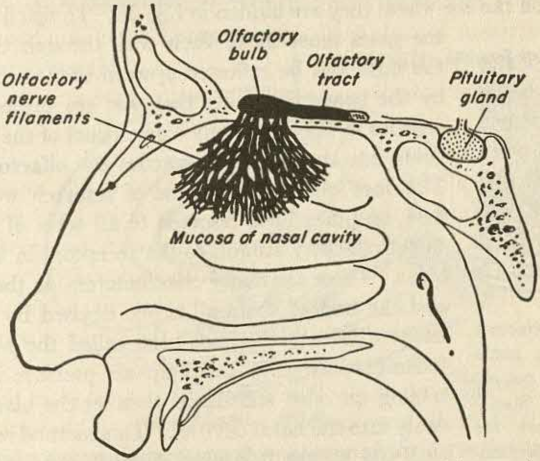

FIG. 38. Drawing of the nasal cavity and olfactory structures. The nose is to the left and the back of the mouth to the right. The diagram exposes the interior of the nasal cavities and shows roughly how the olfactory membrane is spread out in the mucosa of the cavity. Fibers pass through the cribriform plate to join the olfactory bulb, which in turn connects with the brain through the olfactory tract. The pituitary gland is included just as a landmark in the diagram. (*From E. Gardner. Fundamentals of neurology. Philadelphia: Saunders,* 1947. *P.* 204. *By permission of the publishers.*)

It has also been proposed that ultraviolet absorption may be related to olfactory excitability (Heyninx, but see Moncrieff, page 302). As Moncrieff points out, there are exactly the same difficulties with this theory as with the infrared theory.

Finally worth mentioning is what may be called the Raman shift theory (Dyson). The Raman shift is an optical phenomenon in which a substance radiated by light of one wave length may give off wave lengths both shorter and longer than the original light. This happens under special optical conditions, which we need not go into. The difference between the wave length of light with which the substance is irradiated and the wave length that it scatters is called the Raman shift. Like infrared and ultraviolet absorption, it is a measure of molecular activity. There may be something in the notion that the Raman shift has some fundamental relation to olfactory excitability. We cannot be sure at present. It is claimed, however, that all substances with odors have a Raman shift between 140 and 350 mμ (see page 148 for explanation of mμ). Moreover, it looks as though substances with a similar Raman shift have similar odors. Exceptions may eventually be found which may dislodge this theory, as they have others. At present it looks promising.

The Olfactory Cavity. So much for notions about the stimulus and olfactory quality. Let us now turn briefly to the neurosensory apparatus of olfaction.

The olfactory receptors are tucked away in alcoves at the roof of the nasal cavities. You can see where they are hidden in Fig. 38. To reach the receptors the gases must make their way through the nostrils of the nose and be reflected upward to the olfactory region by the bones (conchae) that you see projected into the cavities in Fig. 38. Only a small part of the gases and air going into the nose ever reaches the olfactory receptors. This fact has been the bane of research workers in the field, and they have resorted to all sorts of contrivances to get olfactory stimuli to the receptors in known quantities. There are many olfactometers, as they are called, and the best of them all is one devised by Elsberg and Levy. Their method has been called the blast-injection technique, for they build up air pressure in a jar containing an odor substance, then let the blast of air suddenly into the nasal cavities. This method seems to work well and to get measured quantities of stimuli to the olfactory membrane (Jerome).

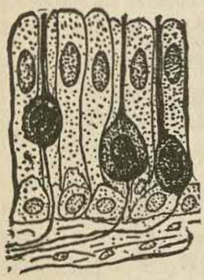

FIG. 39. The olfactory epithelium, or membrane. At the bottom are basal cells. Standing upright are the supporting sustentacular (columnar) cells. The olfactory receptor cells are the oval cells with the long hairs. (*From H. L. Wieman. General zoology. New York: McGraw-Hill, 1925. P. 221. By permission of the publishers.*)

The Olfactory Epithelium. Usually about 500 sq. mm. in size, the olfactory epithelium (Fig. 39) in man can be distinguished by the sharp, although irregular, boundary that it makes with the adjacent epithelium and by its typically yellowish or (in some animals) brownish color. It is composed of three types of cells: (1) the pigmented *columnar* cells, which are sandwiched between the olfactory cells and whose function is plainly one of support; (2) the *basal* cells, which are blocklike in form and are located on the innermost surface of the epithelium, thereby providing the groundwork to which the rest of the epithelium is attached; and (3) the more numerous *olfactory* cells proper. The outer portion of these olfactory neurons consists of fine filaments, or 'hairs,' the middle portion is the cell body, and the inner part tapers off into axons conducting excitation away from the epithelium. Passing upward through the bony *cribriform* plate, from which the epithelium hangs, these fibers end upon the second-order neurons of the olfactory bulb. This structure lies just above the cribriform plate.

The outer surface of the epithelium is bathed in a mucous fluid secreted by the epithelial cells of the nasal cavities. It seems quite probable that all gases must be soluble in this fluid to be able to excite the olfactory receptors. It also looks as though excitation takes place in the hairs of the olfactory receptors. The truth of the matter is, however, that we know practically nothing about the way in which gases entering the nasal cavity come to arouse nerve impulses in the olfactory system.

Neural Centers and Pathways. Despite the fact that smell is of very little use to man, none of the senses presents such a complicated neural system as does olfaction. It is impossible to show all its relations clearly in a simple diagram. The diagram you see in Fig. 40 indicates some of the principal parts seen on the ventral and medial surfaces of the brain. Accounting in part for the apparently needless complexity of the olfactory system is the fact that smell was very important and highly developed in many of the lower animals. Man seems to carry over this system in its complexity, even though he has little use for it.

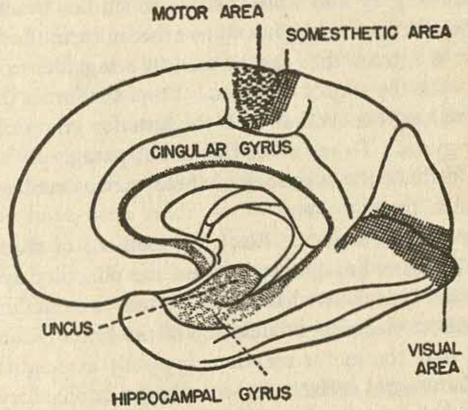

FIG. 40. Mid-line view of the cerebrum showing some of the connections of the olfactory system. The ventral areas receiving the olfactory tract lie in a complex arrangement covered somewhat by the temporal lobe and are not shown. The hippocampal gyrus and uncus, which connect with the ventral areas, are shown. So is the cingular gyrus. (*After S. W. Ranson. Anatomy of the nervous system. Philadelphia: Saunders,* 1941. *P.* 282. *By permission of the publishers.*)

As you have already seen, axons from the olfactory epithelium pass through the cribriform plate to the olfactory bulb. This bulb, an extension of the brain, is itself rather complex. One of its chief features is the *glomeruli*, which are bushy networks of fibers upon which olfactory axons end and from which arise fibers going into the brain. Another feature of the bulb is its networks of reverberatory circuits. Axons from one neuron stimulate a second neuron, which in turn excites the first neuron. This reverberatory system, like similar systems elsewhere in the brain and spinal cord (see page 75), allows impulses to continue after a stimulus has ceased, and it also provides a sort of amplifying system which probably increases the sensitivity of the organism to olfactory stimuli.

From the olfactory bulb, fibers pass toward the brain in the *olfactory tract.* This breaks up into three divisions which go, respectively, to (1) the ventral olfactory cortex, (2) nuclei in and around the hypothalamus, and (3) the parolfactory area of the cerebral cortex. This latter area is located deep within the longitudinal fissure near the corpus callosum and the cingular gyrus (Fig. 40). The ventral olfactory cortex sends fibers, it is thought, to the *hippocampus*, a complex structure of gray and white matter which lies beneath the cortex of the temporal lobe. From the hippocampus arise, in turn, fibers which make up the *fornix.* This is a tract that can be seen in a saggital section of the brain running just beneath the corpus callosum. From the fornix there appear to be relays of fibers making connection with the anterior group of thalamic nuclei and the cingular gyrus. To say all of this in one paragraph is going a bit fast, but we know so little of the functions of these various centers that we should not spend too much time on them.

Electrophysiological Functions. Electrical methods of studying brain functions have recently been brought to bear on the olfactory system. We need more studies of this type, but what there are tell us something. One experiment employed direct electrical stimulation of the brain (Rioch and Brenner). It demonstrated that the motor reactions typically associated with odors are represented on the ventral surface of the brain in the olfactory centers located there. Salivation, chewing movements, chop licking, and sometimes sniffing can be elicited by stimuli applied to the ventral region. This experiment tells us that the ventral areas, which receive impulses from the olfactory bulbs, not only have sensory functions but control some of the behavioral reactions to smell as well.

Recording of electrical potentials from olfactory centers also gives some interesting results. This was first done systematically in the hedgehog, a lowly mammal but one in which the ventral surfaces of the brain are a bit more accessible than they usually are (Adrian). One point of interest is that there were potential waves in both the olfactory bulbs and the pyriform area during normal breathing of the animal or when air was forced into the cavities. Each breath or blast gave rise to a train of waves of 15 to 45 per second. This would seem to mean either that pure air has an odor but we are unaware of it because we live in it (?) or that there are also receptors to mechanical stimulation in the olfactory region and system. As one might expect, the use of olfactory stimuli such as clove oil or asafetida produced marked electrical responses in the bulbs and pyriform area. If the stimulus was intense it produced a continuous series of small waves at a frequency of about 50 per second.

There is a second study, carried out in the cat (Fox *et al.*), in which electrical methods of recording were also used. In this one the stimulus also was electrical, rather than chemical, and was applied to the olfactory bulb in single shocks. Electrical reactions to such shocks were picked up in the olfactory tracts, the olfactory tubercle, and the pyriform areas. These responses are what one might expect from our earlier description of the anatomy of the olfactory centers. Striking, however, was the fact that no responses could be obtained from the hippocampus, a large structure long thought to be olfactory in function, nor from the region of the septum in which the cingular gyrus and fornix are located. Nor could responses be obtained from the amygdaloid nuclei. All these structures appear anatomically to have olfactory functions, but failure to find electrical responses in them casts doubt on this belief. Some results that we shall take up later in connection with the expression of emotion also raise doubts whether the amygdala and cingular gyri are really olfactory centers. Indeed, the olfactory centers may not be as extensive as we have thought. They may be confined to the olfactory tracts, the pyriform areas, and some minor tracts connected with them.

Behavioral Functions. There are a few additional experiments in which behavioral measures have been used. In each case the animal was required to make a discrimination or a conditioned response to olfactory substances, after which parts of the brain were removed to see what effect their removal had on these responses. The experiments are easily classified into two groups: those dealing with ventral olfactory structures and those concerned with thalamocortical relationships in olfaction.

Ventral Structures. The experiments on ventral structures were done with dogs. In one, the hippocampus was bilaterally removed (Allen). There was no effect on conditioned foreleg responses of the dog to clove oil vapor. In another experiment, the amygdaloid nuclei and the pyriform areas were removed together and, in certain cases, in combination with the hippocampus (Allen). In none of these cases was there any interference with the animal's ability to respond to the presence or absence of odors. From these experiments it is not possible to conclude that the amygdala, the pyriform area, and the hippocampus are not concerned in olfaction. One can say, however, that they are not essential to olfactory responses. Not involved in these experiments were the median olfactory pathways to the hypothalamus and thalamus. These were probably the pathways that functioned in the normal responses of the dog after removal of the other centers.

Thalamus and Cortex. Finally to consider are some experiments on the thalamocortical system, all of them done with rats. In two experiments rats were able to make an olfactory discrimination after part of the cerebral cortex was removed (Ghiselli and Brown, Swann). Some of the lesions were large ones. It is probably fair to conclude that no part of the neocortex outside of the ventral areas is essential for olfactory sensation. To check on this point a little more specifically, Lashley and Sperry did another discrimination experiment with rats in which they severed the cortical radiations coming up from the anterior group of thalamic nuclei. These are the nuclei that anatomists have thought received olfactory pathways from below and conveyed them to the neocortex. In the experiments, however, there was no effect of severing these radiations on olfactory discrimination.

To sum up these various experiments, we have not yet put our finger on the centers of either the ventral cortex or the neocortex that may be essential for olfaction. We know that impulses arrive in the pyriform areas, but it is a question whether the amygdala, hippocampus, or other 'higher' structures have anything to do in smell. Obviously a great deal of further research is in order to tell us just what centers and pathways perform what functions in our sense of smell.

Brain Lesions in Man. It would be well to mention in passing the use of olfactory tests in the diagnosis of brain lesions. The blast-injection technique for obtaining olfactory thresholds has been used for that purpose on a large scale (Elsberg and Spotnitz). In such diagnostic tests an elevation of the threshold for coffee or citral odors is taken to indicate pressure or damage to the olfactory bulbs or tracts. Lengthening of the time of adaptation, normally between 30 sec. and 4 min., is supposed to indicate some kind of interference with the olfactory centers of the brain proper. Over 1,000 neurological patients have been examined with this technique. Thirty-four per cent of the patients showed no olfactory disturbances. About 40 per cent of the patients having damage in the frontal or temporal lobes showed disturbances of threshold. From measures of fatigue, lesions were correctly identified in 54 per cent of the cases and incorrectly diagnosed in 18 per cent.

GUSTATION

Now let us turn to the third of the chemical senses. We shall speak of it sometimes as *gustation* and sometimes more simply as *taste*. In taking up this sense we shall pass by quickly the points on which there is confusion and controversy and put the greatest emphasis on those facts and experiments which seem to have the greatest importance for understanding the physiological basis of taste.

The Taste Receptors. We have already noted that the taste receptors, in contrast to those for smell, make use of a specialized epithelial cell supplied with nerve endings. This cell is called a *taste cell*. Such cells are located in a more complex structure of cells called a *taste bud*. Such a structure, shown in Fig. 41, is a flask- or bud-shaped cluster of cells embedded in the ridges (papillae) of the tongue. Many of the cells of the taste bud seem to be there to support the sensory taste cells. Solutions in the mouth containing stimuli for taste get to the taste cell by penetrating a pore in the taste bud and the spaces between the cells of the taste bud.

It is significant, perhaps, that the integrity of the taste cells, sometimes called 'secondary sense cells,' depends upon the primary sense cell, the neuron, which serves it. In the embryonic development of the individual, it is the primary neuron that causes the epithelial cell to differentiate into a taste cell. Moreover, the process is reversible, for sectioning the nerves for taste after differentiation has taken place causes the taste cells to change 'backward' toward more primitive epithelial cells (Olmsted). This phenomenon of control of the structure of the epithelial cell by the primary neuron has been called *sensory appropriation*. It indicates, perhaps, that there are some chemical influences or neurohumors of the primary neuron that induce the specific changes in the epithelial cells.

Gustatory Sensitivity. Even a casual observation of the structure of taste buds makes it clear that there must be two stages in the process of exciting taste receptors. One is penetration of the taste bud by the chemical stimulus. The second is the chemical reaction, presumably, through which nerve impulses are set off. Both are important in taste sensitivity.

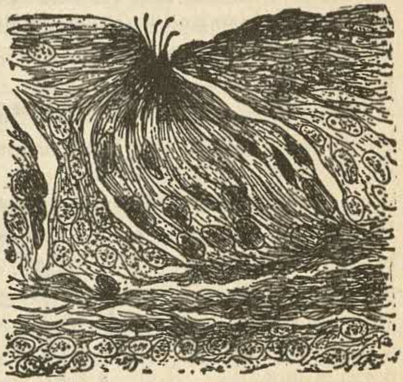

FIG. 41. Structure of the taste bud. Most of the cells (those with light nuclei) are supporting cells, which surround the sense cells somewhat like a barrel stave. The sense cells are those with the darker nuclei, and some can be seen to the right. These cells, largely within the bud, have hairs on them that project up through the taste pore. Innervating the sense cells are some nerve fibers, which are shown as streaming from the lower right-hand corner of the drawing. (*After Ranvier. From P. H. Mitchell. A textbook of general physiology. 4th ed. New York: McGraw-Hill, 1948. P. 189. By permission of the publishers.*)

Penetration is a factor in the time required for appreciating gustatory stimuli. It usually takes some time to sense taste stimuli. If, for example, one applies a salt solution of 3*N* concentration, it will be about 10 sec. before the sensation of salt reaches a maximum of intensity. Penetration is an important factor in this delay. It also accounts in part for our sensitivity to different kinds of substances. In certain of the lower animals there are changes in the color of tissues when acid substances have penetrated the tissue cells. This fact has been put to use in studying the factors governing cell penetrability (Crozier). The several experiments in this line point to several factors governing cell penetrability. One of them is the degree to which a substance ionizes in solution. Another is the size of the molecule. Another is whether the substance is an organic (containing carbon) or inorganic material. And there are certain physicochemical aspects of the solution that are important too. A knowledge of these various factors will allow an investigator to predict with considerable accuracy the taste thresholds of an individual to different substances.

A second factor determining taste sensitivity seems to be the different types of taste receptors that exist for different stimuli. This point, however, is better considered under the general topic of taste qualities.

Taste Qualities. As in smell, vision, hearing, and the skin senses, many theorists and investigators have attempted to apply the classic doctrine of specific nerve energies to the problem of taste sensation. They have supposed that there are a few basic qualities of taste sensation of which all other sensations are mixtures and that these qualities depend on a corresponding number of specific taste receptors.

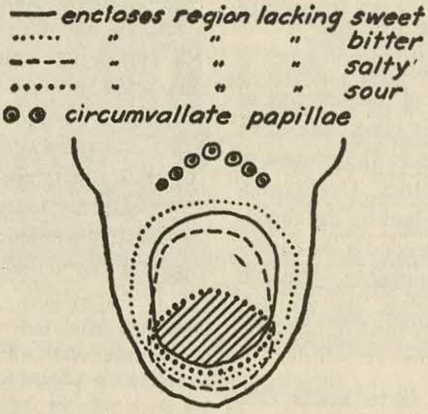

FIG. 42. Regions of the tongue in which sweet, bitter, salty, or sour sensitivity is lacking. (*From R. S. Woodworth. Experimental psychology. New York: Holt,* 1938. *P.* 497. *By permission of the publishers.*)

People agree fairly well now, and the evidence seems to support them, that there are four fundamental taste qualities. The names for the four experiences are *sour*, *salt*, *sweet*, and *bitter*. There are six different lines of evidence, which we can run over quickly, that make us think these four are the correct ones: (1) Qualitative differences in subjective experience fall rather definitely into four such categories. (2) Experiences that cannot be so classified can be explained in terms of the stimulation of tactual or common chemical receptors. (3) Individual papillae can be found on the tongue that give rise, when stimulated, to a single quality of experience. (4) The areas of the tongue in which each quality may be aroused are not coextensive but fall into four rather distinct zones (see Fig. 42). (5) Some drugs, applied to the tongue, eliminate one quality of experience while leaving the others relatively unaffected. (6) One can reproduce fairly accurately the taste of any substance by mixing typical sweet, bitter, salt, and sour stimuli in appropriate proportions.

The Chemical Basis of the Qualities. Considerable effort has been expended to determine precisely what groups of chemicals are correlated with the qualities of taste experience (see Crozier, Moncrieff). The unanimity of many investigators in finding the hydrogen ion (H^+) of acids to elicit 'sour' leaves little question about its importance in this taste quality. Even in 'salt,' however, the matter is not so simple, for more than one ion or atom is able to elicit it. In general, the inorganic salts, particularly the halides (chlorine, iodine, and bromine) of sodium, potassium, ammonium, lithium, and magnesium are most effective, and it has been suggested that the halides, in ionized form, are responsible for 'salt.' Not in accord with this generalization, however, is the fact that the nitrates (NO_3^-) and sulfates (SO_4^-) also are capable of evoking 'salt.' Perhaps it is better to say that the negative ion (anion) is the chemical basis of 'salt'; but this statement, too, has some exceptions, and it is not known whether they can be accounted for in terms of the factors of penetrability noted above.

'Bitter' is closely allied with a family of complex chemical substances known as the alkaloids. Their basic properties appear to be due to amino groups (NH_2) or to trivalent nitrogen atoms ($N^{\equiv}$). Many substances, on the other hand, which are not alkaloids and which may be quite unrelated to them chemically, evoke 'bitter.' Some of the inorganic salts are examples. No simple chemical property, therefore, can be said, as matters now stand, to be the basis of 'bitter.' Much the same statements apply to 'sweet,' although the sugars are the class of substances most notable for their sweetness. Our failure so far to find a limited number of chemical properties correlated with sensory qualities should not, however, dismay us, for we also need to know what the receptive substances in the taste cells are. Without knowing them we cannot expect to make much progress in discovering the important properties of the stimulus, for these, it seems obvious, must be determined also by the chemical nature of the receptive substances and the types of chemical reactions in which they can participate.

Specific Fibers for Taste. Although we may not know exactly what chemical groupings go along with the four basic taste qualities, we now have some idea of how the different receptors sort out different stimuli. This idea comes from some brilliant and decisive experiments with electrical responses in individual fibers of the taste nerves. Pfaffmann, their author, first succeeded in teasing out individual nerve fibers from the gustatory nerves of the cat. Then he placed electrodes on these fibers so that he might record nervous impulses in them. Once a fiber responded when he stimulated a spot on the tongue, he applied four different kinds of stimuli to that spot: acid (for sour), salt, sugar (for sweet), and quinine (for bitter)—the four kinds of stimuli for the classic qualities.

The exciting thing about the experiments was that different fibers responded to different stimuli. He could get no responses in any fibers to stimulation with sugar. That proves nothing, for it might have been his bad luck in not picking up the right fibers. He could find three different types of fibers responding to the other three kinds of stimuli, but the way in which they did it is not quite what you might expect. All fibers responded to acid stimulation. Some fibers, however, would respond only to acid and not to salt or quinine. Other fibers—a second class—would respond to salt as well as to acid, but not to quinine. And a third class would respond to quinine and acid, but not to salt.

It is the fact that all fibers responded to acid that was unexpected. It makes us give up the simple classic theory that each type of receptor responds to one and only one type of stimulus. On the other hand, the experiment gives a firm basis to a specific-receptor theory of quality—the general notion known as the *doctrine of specific nerve energies*—that the quality of our experience is determined by the receptors that respond. The modern version, at least for taste, is that the pattern of fibers responding is the basis for sensory quality. Thus an acid stimulus excites all three types of fibers, a salt stimulus only one, and a quinine stimulus only one. Or, in Pfaffmann's own words,[1]

> If we carry over this mechanism [from the cat] to the human, we might say that a discharge of impulses in one set of fibers will produce salt, whereas discharges in the same fibers combined with activity in all the remaining gustatory fibers produce sour. In such a system, sensory quality does not depend simply on the 'all or nothing' activation of some particular fiber group alone, but on the pattern of other fibers active.

We must be careful, Pfaffmann points out, not to assume that the three types of fibers found in the cat are all that exist either in the cat or in man, for his stimuli were limited in number. The results, nevertheless, appear to provide a sound basis for a conception of the mechanism of gustatory quality.

Neural Centers and Pathways. We can turn now to some of the higher centers of the taste system. Branches of three different cranial nerves serve the taste buds: the VIIth, IXth, and Xth. All of these, after passing through their respective cranial ganglia, end up in the medulla or pons of the brain. Here the fibers are collected in a tract, the *solitary tract*, which runs a short distance posteriorly and ends upon the second-order neurons of the solitary nucleus. It is interesting to note in passing that the solitary tract and nucleus, although relatively small in man, are extremely large in some fishes—so large, in fact, that they form large lateral lobes on the medulla called *vagal lobes*. In these fishes taste is quite important. Indeed, the taste buds are not limited to the tongue and mouth but are distributed liberally over most of the body surface. This distribution correlates with the large size of the bulbar centers for taste.

From the solitary nucleus, fibers run forward in the brain toward the thalamus in a tract called the *medial lemniscus*. It is easy to lose track of these fibers when purely anatomical methods are used, and it was thought for a long time that they ended up in some regions associated with the olfactory system. This theory, however, forgot the fact that taste is more closely associated with the skin senses than with smell—at least in its embryological and evolutionary development. Taste starts out in fishes being distributed over body surfaces, and like the skin senses, it develops by inducing differentiation in epithelial cells. It turns out now that this association with the skin senses is preserved in the higher centers of the brain, for taste tracts from the medulla end up in the posteroventral nucleus of the thalamus—the part concerned in the skin senses. The projections for taste continue with those from the skin of the face and mouth to the cortex.

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[1] Page 255.

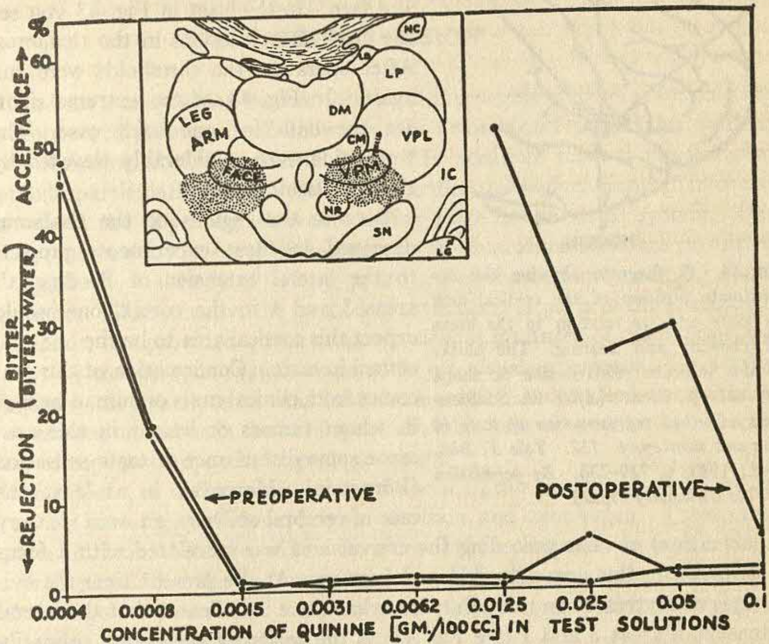

FIG. 43. Taste discrimination of quinine before and after injury to the facial portions of the posteroventral nucleus of the thalamus. The dotted area in the inset shows the region of injury in the thalamus. For the meaning of other letters in the drawing, see page 42. (*Courtesy of T. C. Ruch. Based on work of H. D. Patton, T. C. Ruch, and A. E. Walker. Experimental hypogeusia from Horsley-Clarke lesions of the thalamus in Macaca mulatta. J. Neurophysiol.*, 1944, 7, 171–184.)

Behavioral Functions. These points about the thalamic and cortical representation of taste have been established by experiments with monkeys and clinical observations in man. Monkeys, like men, do not like quinine because of its extreme bitterness. This fact was used to carry out some experiments with monkeys (Patton and Ruch, Blum *et al.*). Monkeys were presented with containers of water, which had graded concentrations of quinine in them. By determining the concentration of quinine solution that they could discriminate just well enough to avoid, thresholds for 'bitter' could be determined. Two examples of such thresholds are shown in Fig. 43. When the threshold determinations were complete, lesions were made in the posteroventral nucleus (see page 42), which projects to the cortical area concerned in sensations of the mouth and face. In the inset in Fig. 43 you see the place of such lesions in the thalamus. After operation the thresholds were run again. In Fig. 43, at the extreme right, are the data for one such case. The thresholds were considerably elevated by these thalamic lesions.

Because the regions of the thalamus damaged in these experiments projects to the lateral extension of Brodmann's areas 3 and 1 in the cortex, one would expect this cortical area to be the one concerned in taste. Confirmation of this fact comes from clinical cases of human beings, in whom tumors or lesions in this area cause some disturbance of taste sensation (Börnstein). Moreover, in at least one case of cerebral epilepsy, an aura (sensory hallucination) of taste preceding the convulsions was correlated with a focus of irritation in this area (Shenkin and Lewey). At the present time the evidence is not extensive on this point, but what there is indicates that the lateral extension of areas 3 and 1 (see Fig. 44) is the region of the cortex primarily concerned in taste.

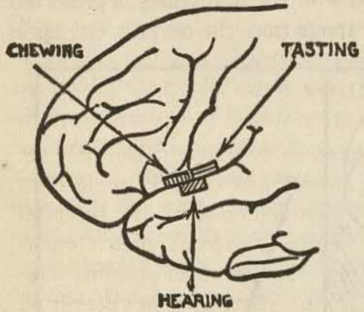

FIG. 44. A diagram showing the approximate position of the cortical area for taste and its relation to the areas for chewing and hearing. The blocks do not indicate relative size or shape but only position. (*After W. S. Börnstein. Cortical representation of taste in man and monkey, p.* 732. *Yale J. Biol. Med.*, 1940, 6, 719–736. *By permission of Yale University Press.*)

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CHAPTER VII

SPATIAL VISION

Of all the senses, vision has been the most thoroughly studied. Not only are its centers and pathways well known, but its neurons and synaptic connections have been described in accurate detail. In addition, modern physiological methods, particularly those of electrical recording, have given us much information about the physiological events taking place in the visual system. Our ability, moreover, to control various aspects of visual stimulation has permitted us to gather a vast body of strictly quantitative information concerning visual experience. Then, finally, the method of extirpation of parts of the brain, used in animals, has provided direct means in several instances of discovering the centers of the nervous system responsible for visual experience. To survey adequately all this material would require a volume, and, indeed, several have been written on it; but in the brief space available here we are limited to a summary of the most important aspects of vision.

The subject, as well as what we know about it, can be divided conveniently into three parts: spatial vision, brightness vision, and color vision. These three aspects of vision, therefore, will be the titles of three chapters. In each of them we shall summarize the anatomy and physiology that are basic to the topic and then go on to consider the perceptual phenomena and the physiological mechanisms that underlie them.

THE EYE

The chief feature of the anatomy of the eye is that it is so constructed as to be able to perform the functions of a camera (see Fig. 45). Inside the eye is its photosensitive plate, the *retina*, and protecting this plate from stray light is a pigmented *choroid* coat of tissue, which surrounds the eye except in front, where the transparent *cornea* admits light. Such light must pass, as must the light entering a camera, through a small aperture, the *pupil*, and then through a *lens*, which by means of its curved surfaces so bends light that it is brought to a focus on the photosensitive retina. Unlike the arrangement in a camera, however, is the fact that the light, in its course from the cornea to the retina, passes through a semifluid, but transparent, *humor*. The eye, moreover, is more adaptable than a camera, for muscular regulation of the size of the pupil and the curvature of the lens controls the amount of light admitted to the eye and the clearness of the retinal image, whether the object it reflects is near or far.

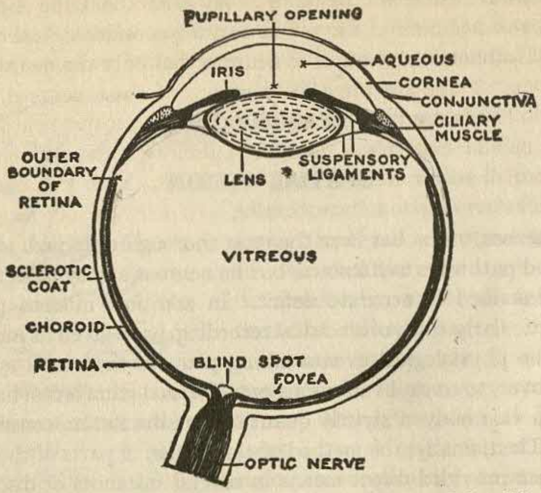

FIG. 45. A diagram of the eye. *(From H. C. Warren and Leonard Carmichael. Elements of human psychology. Boston: Houghton Mifflin, 1930. P. 80. By permission of the publishers.)*

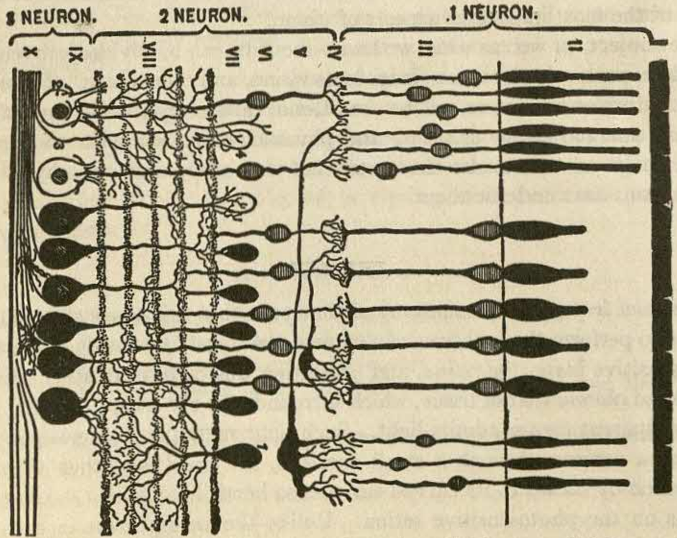

FIG. 46. Diagram of the cellular relations in the retina. *I*, Pigment cells lying next to the choroid coat; *II*, layer of the rods and cones; *V*, layer of horizontal cells; *VI*, bipolar cells; *IX*, large ganglion cells; *X*, axons of the ganglion cells uniting to make up optic nerve. *(After Greeff. From J. F. Fulton (Ed.), A textbook of physiology. 16th ed. Philadelphia: Saunders, 1949. P. 438. By permission of the publishers.)*

Retinal Layers. There will be more to say later about the effect of light in the eye, but the structure of the retina may be considered first (Fig. 46). It is made up of supporting cells and of neurons, but only the neurons are of importance to us. There are three main groups of these neurons, arranged in three layers. The first group is a row of primary receptive neurons, the sense cells, facing toward the outside of the eyeball; their receptive portions have taken the highly specialized forms of *rods* and *cones* in which are contained the chemical materials responsive to light. Making synapse with such sensory neurons are the *bipolar* neurons of the second layer, and these bring impulses to neurons of the third group, the *ganglion* cells. The axons of these cells run over the inner surface of the retina and are collected at one point, the *blind spot*, somewhat medial to the center of the retina, where they leave the eyeball and proceed as the optic nerve to the visual centers of the thalamus and midbrain. Thus the visual organ is made up, essentially, of photoreceptor neurons, intervening bipolar cells, and ganglion cells, with the latter transmitting messages directly to the brain.

Lateral Neurons. Knowledge of other details of retinal structure is also necessary for understanding visual functions. The retina, we have noted before, is an outgrowth of the brain, and careful study of its structure has shown that it fully demonstrates this kinship (Polyak). All the cells of the retina, described above, are true neurons, and their various synaptic connections appear to be as complex as many in the brain. First of all, the bipolar cells often collect from several rods and cones, and these also frequently deliver impulses to a number of bipolar cells; thus neural effects arising in the rods and cones both diverge and converge in their transmission from receptor cells to ganglion cells. There are, moreover, at least two types of 'association' cells which serve further to interconnect the activity of receptor cells: *horizontal* cells pick up from some receptor cells and deliver to others; and in the inner part of the retina *amacrine* cells spread impulses aroused by bipolar cells to several ganglion cells or, in some instances, return excitation from bipolar elements to the receptors. The functional system set up by these various interconnections, as the reader can see, permits all sorts of mutual influences between various layers and adjacent parts of the retina. In this respect the retina appears to be very much like the brain.

Rods and Cones. Going on to other details of the retina, we may note a fact verified by many histologists, that the rods and cones constitute two distinct types of receptor cells. Their connections with bipolar and horizontal cells, however, clearly indicate that they do not form two distinct systems as has frequently been assumed (Polyak). Bipolar cells often collect from both rods and cones, and so also do horizontal cells (see Fig. 46). We may expect, therefore, that the activities of rods and cones will be intimately related in visual functions.

Fovea and Periphery. Of considerable significance is another fact, that synaptic interrelationships of the retinal cells vary according to different areas of the retina. In its center is a rod-free area, the *fovea*, in which each cone is served by one bipolar cell, and vice versa. Here, therefore, we may expect little or no interdependence of the functions of adjacent receptors. Proceeding outward from the fovea, we find more and more of the synaptic interrelationships described above. The number of cones, moreover, diminishes, whereas the rods become more numerous; in the extreme periphery only rods prevail, and these are associated with bipolar cells in ratios as high as 200:1. Thus in moving from the center to the periphery we find two changes: from a predominance of cones to one of rods, and from point-to-point to diffuse synaptic connections.

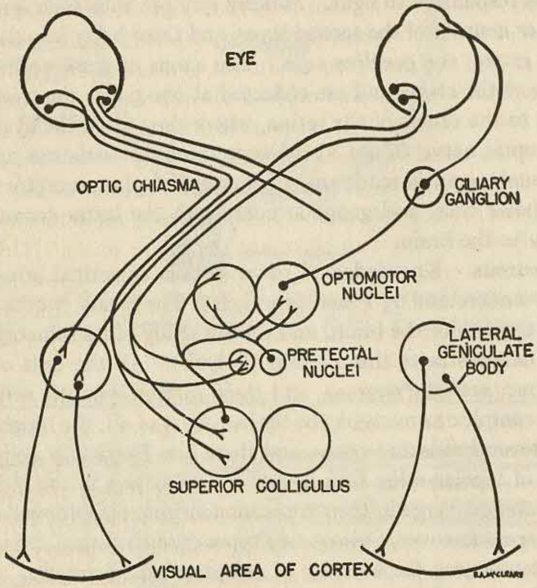

FIG. 47. Diagram of the centers and pathways of the visual system.

THE CENTRAL VISUAL SYSTEM

The Optic Nerves. The two optic nerves, one from each eye, are made up of the axons of ganglion cells of the two retinae (see Fig. 47). Directed backward and medially, the two nerves meet in the *optic chiasma* at the base of the brain just anterior to the stalk of the pituitary body. In animals below the mammals, all fibers cross at the chiasma and end up in opposite sides of the thalamus or midbrain from the eye of their origin. In mammals, however, the fibers from the more lateral parts of the retina remain uncrossed; and since the number of uncrossed fibers in the higher mammals is about equal to that of the crossed fibers, the lateral half of the retina is represented in the same side of the brain, whereas the medial half projects to centers of the opposite side.

Subcortical Centers. The *lateral geniculate bodies*, the *superior colliculi*, and the small *pretectal nuclei* lying just in front of the colliculi are the principal places of termination of the optic nerve fibers. Those that end in the lateral geniculate may connect with other cells ending in the other centers. But the main function of the lateral geniculate body, at least in higher mammals, is as a way station to the cerebral cortex. In the geniculate are the cell bodies of neurons whose axons leave it and proceed to the occipital (striate) areas of the cortex in the *optic radiations*. It is upon these cortical areas, we shall see, that the more complex visual functions depend.

More elementary aspects of visual experience, as well as the basic adjustments of the head, eyes, pupil, and lens, depend upon the colliculi and pretectal nuclei. Closely associated with them are the motor nuclei (IIIrd, IVth, and VIth) of the brain stem, controlling eye movements. These nuclei also include the autonomic nuclei effecting changes in the lens and pupil and the pathways to the centers of the brain and spinal cord that give rise to general behavior of the head and body.

Projection in the Visual System. It is often said that in vision there is a one-to-one projection of the retina upon the optic cortex. By this statement is meant that in the pattern of nervous activity reaching the cortex there is a good reproduction of the stimulus pattern falling on the retina. In support of this belief is considerable anatomic and psychological evidence. Patients with a particular part of the visual cortex destroyed tend to display blindness in a corresponding part of their visual field. If, moreover, one deliberately destroys a part of the optic cortex of an animal, cells degenerate in corresponding zones of the lateral geniculate body; a similar result follows destruction of part of the retina. By this method, in fact, accurate maps of the spatial relation of the retina, lateral geniculate body, and optic cortex have been prepared.

These facts testify to the high degree of spatial organization that exists in the visual system, but they do not close the question. When we turn to microscopic studies of synaptic connections such as have been done by Polyak for the retina and Lorente de No for the visual cortex, we see that there is a considerable amount of overlapping of the endings of visual neurons in both the retina and the cortex and, presumably, also in the lateral geniculate body. Indeed, it is fair to conclude that the degree of overlapping is much greater than the degree of acuity found in human and animal vision would suggest and that there must, consequently, be some functional mechanism in addition to the mere spatial organization of synaptic connections to account for visual acuity. To explain such a mechanism for achieving point-to-point projection of impulses in spite of the apparent lack of an anatomical basis for it, Lorente de No has presented an attractive hypothesis based upon demonstrated facts which have been previously reviewed (see Fig. 48).

According to Lorente de No, the discrepancy between anatomical and physiological projection is to be admitted, the latter being pointlike. A point-to-point functional projection, however, can be explained by assuming that the neuron is a summation apparatus, requiring that two or more impulses from other neurons end upon it for it to be activated. Thus, in a situation such as is depicted in Fig. 48, the impulses arriving on the fringe of a group of neurons do not succeed in 'crossing' the synapse because there are no impulses adjacent to them with which to summate, but those in the center of the activated group mutually facilitate transmission by providing several impulses at the same instant at one synapse. Thus, by a mechanism of summation, neuronal activity is kept in discrete pathways when it would spread considerably if anatomical connections and one impulse at each synapse were sufficient conditions for synaptical transmission.

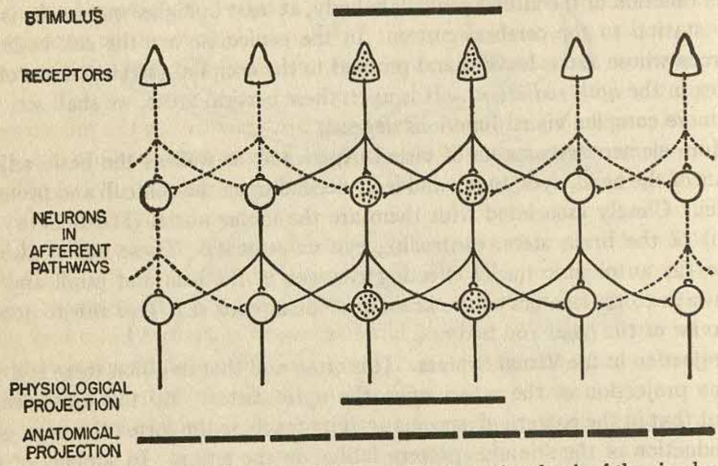

FIG. 48. Diagram illustrating how synaptic connections at various levels of the visual system give relatively diffuse anatomical projection and how, by means of the synaptic summation required in transmission, there can be a point-to-point physiological projection of retinal images upon the visual cortex. (*After Lorente de No.*)

This account, Lorente de No points out, is a much simplified version of what probably takes place. It leaves out such important facts of the visual system as the lateral connections between neurons of the same layer and the possibility of direction inhibition of neurons lying on the boundaries of stimulation. In fact, since Lorente's summation scheme was proposed, we have secured a great deal of evidence that inhibition plays a role in retinal processes. We shall take up some of this evidence later.

THE VISUAL STIMULUS

Although the stimulus for vision, light, can be conceived as made up of minute corpuscles, or quanta, it is usually more useful to think of it as vibratory energy. All the various kinds of light, moreover, may be specified in terms of two variables: the amplitude of the vibration, or the *intensity;* and the frequency of vibrations or its inverse, *wave length,* derived by dividing the speed of light by its frequency. Most light stimulating the eye does not, of course, consist of a single wave length but of many. The light, however, can always be specified, if we have the appropriate equipment for analysis, in terms of the intensity and wave length of the respective components, which together make up the *composition* of the light.

The Measurement of Light. Scales that are practical for the measurement of light are based upon an arbitrary unit, the *international candle,* which is approximately equivalent to the total amount of light emitted by an ordinary candle having a flame about 1 in. in height. One is usually interested, however, not in the total intensity emitted by a light source but in the amount of light falling upon an object. That is *illumination,* and the unit of it is the *foot-candle:* the light falling upon 1 sq. ft. of area placed at a 1-ft. distance from an international candle. Sometimes, however, we would rather know how much light is reflected by an object. This is *luminance,* and one of the most commonly used units of luminance is the *millilambert:* the light reflected by a perfectly diffusing and reflecting surface 1 ft. square and illuminated by 0.93 foot-candle.

Retinal Illumination. Much of the time it is permissible to state the comparative amount of light entering the eye in terms of the luminance of the object viewed. It must not be forgotten, however, that retinal illumination depends upon the size of the pupil through which light enters the eye, and thus one must compute this illumination from a knowledge of the brightness of the viewed object and the pupil size. Since the size of the pupil is in turn dependent upon retinal illumination, it is better to use an artificial pupil that is smaller than the real pupil ever is even at extremely intense illuminations.

The regulation of the size of the pupil, we may note, is a reflex affair. The chief center regulating it is the superior colliculus, which, as described above, receives fibers from the retina. From the superior colliculus there are two pathways back to the muscles of the iris. One goes to the region of the oculomotor nucleus and thence to the iris by way of parasympathetic nerves, thus causing contraction of the pupil. The other passes down the spinal cord and out through sympathetic nerves; discharges in this pathway dilate the pupils. The former pathway is activated by high retinal illuminations, the latter by darkness.

The Retinal Image. The eye, we have seen, functions like a camera and is so constructed that an image of external objects is formed on the retina. The retinal image, moreover, is kept in focus when objects are far or near, bright or dim, a feat that is accomplished by two mechanisms, the pupil and the lens. As in a camera, so in the eye: the narrower the aperture, the sharper the focus of the retinal image. The focus, accordingly, is best when the illumination is high and the pupil contracted as a result. To adjust the image for best focus according to the distance of the viewed object, it is necessary that the curvature of the lens be changed. This is done by reflex mechanisms controlling muscles attached to the lens, and in man the pathway seems to consist, to put it briefly, of the lateral geniculate, the visual cortex, and paths down to and out from the midbrain, although in some of the infrahuman animals the mechanism is probably entirely subcortical.

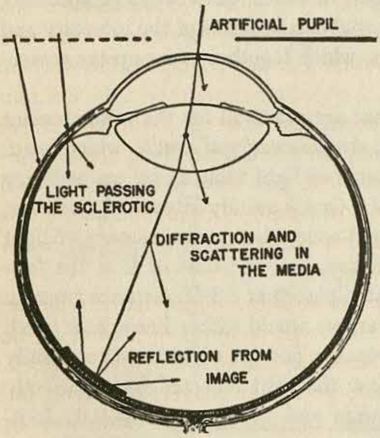
ARTIFICIAL PUPIL
LIGHT PASSING THE SCLEROTIC
DIFFRACTION AND SCATTERING IN THE MEDIA
REFLECTION FROM IMAGE

FIG. 49. Points in the eye at which light may scatter. (*After S. H. Bartley. Vision. New York: Van Nostrand*, 1941. *P.* 58. *By permission of the publishers.*)

Even with these two devices for adjusting the focus of the retinal image, it is by no means so nearly perfect as it might be. There are at least three principal ways in which an otherwise well-focused image will be blurred by the scattering of light (Fig. 49). (1) The internal media of the eye will diffract light, even as moisture in the air distorts and makes the appearance of objects hazy. (2) The retina and internal surface of the eye are light in color and can reflect light to other parts of the eyeball. (3) Some light can penetrate into the eye through its walls. As a result there is always a good deal of stray light in the eye, which affects unfavorably the clearness of the retinal image. In some cases the 'unilluminated' part of the retina may be about 3 per cent as bright as the bright part of the image (Bartley).

VISUAL ACUITY

There are many more things to say than we have already said about the structures of the eye and their physiological function. In later chapters we will say more about them. For the present, however, we have covered enough of the facts about the visual system to take up the spatial aspects of visual perception.

Under the topic of spatial vision we may include any visual perception or visual reaction that makes use of the spatial distribution of light on the retina. The principal items falling in this category are visual acuity, optokinetic reactions, form perception, size perception, and movement perception. We shall take up each of them in turn, defining them as we go along. The first to consider is visual acuity.

Measures of Visual Acuity. If the term meant what it appears to mean, measurement of visual acuity would refer to any sort of test of the 'acuteness' of vision, in fact, any measure of the best visual discrimination that you might make. In practice, however, the term refers to only one sort of acuity, the discrimination of visual objects—the smallest object you can see. Even this sort of acuity can be measured in several ways. One is the common eye chart, used in large-scale eye examinations, in which you must identify the letters of the alphabet when they are as small, or as far away, as possible. Two other ways, which are more often used in laboratory experiments because they are more reliable and more basic measures, are the minimum separable and minimum visible acuity tests. In the minimum separable test, you look at two black lines separated by a white strip, or simply two white dots, and then reduce the space between them to the point where they seem to be one, *i.e.*, until you cannot tell that they are separate lines or points. In the minimum visible test, you view a single line against a uniform background and reduce the relative size of the line until you can no longer see it.

The measure of visual acuity is always the smallest object that can be seen by any of these methods. To express the result in terms of a common denominator that is independent of the particular distance and the particular size that happened to be used in the test, we always convert the result into visual angle, *i.e.*, the angle of the object that can just be seen. Moreover, because the larger the angle, the poorer the vision, and vice versa, it is customary to take the reciprocal of the visual angle of the object that can just be seen as the final way of stating acuity.

As you might imagine, the kind of test that is used affects the results one gets. Whenever two lines or two dots are used (minimum separable method), visual acuity, expressed in terms of the reciprocal of visual angle, is usually poorer than in the test using a single line or a single dot of light (minimum visible). In normal eyes the threshold of visual acuity may vary between 20 seconds of arc and 0.5 second, a factor of 60 times, depending on the technique used. As you will see in a moment, it is easy to understand the differences in results in terms of what goes on in the eye in the course of the measurement of visual acuity.

Minimum Separable Acuity. In Fig. 50, you see a curve showing values of visual acuity (reciprocal of the minimum separable stimulus) for different levels of illumination. Note that the abscissa of the graph is labelled as log millilamberts. This is a common method of expressing visual functions, and it is well to understand what it means. Millilamberts, as we pointed out earlier, are the units of luminance, the light from the object viewed. The logarithmic scale is the scale that we must use for many sensory functions, especially those in vision and hearing, because the nervous system seems to work logarithmically, rather than linearly, in psychological matters (see Chap. X). On the log scale, one unit represents a factor of ten times. Thus −3 log millilamberts is ten times as intense as −4 log millilamberts, and 2 log millilamberts is ten times as intense as 1 log millilambert. You will notice that the abscissa covers a total range of 8 log units, which means that it covers a range of luminance of 10^8, or 100,000,000 times.

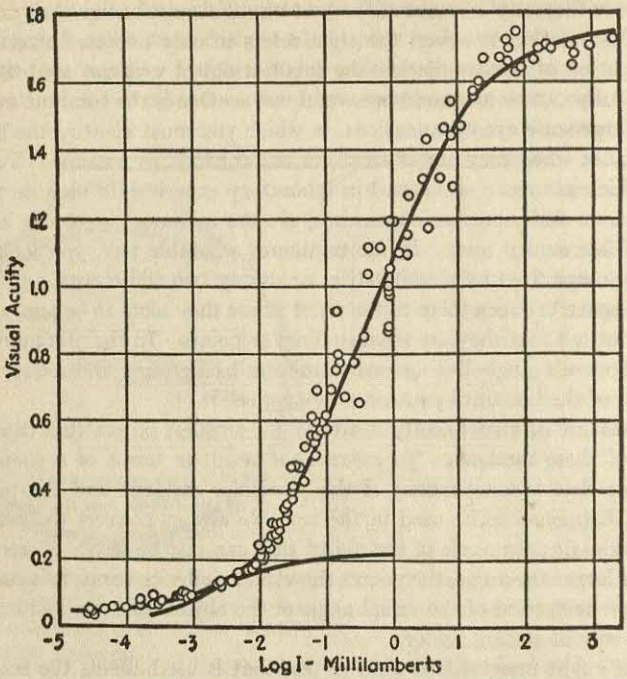

FIG. 50. The relation of visual acuity to intensity of illumination in the human eye. *(From S. Hecht. Vision: II. The nature of the photoreceptor process. In C. Murchison (Ed.), A handbook of general experimental psychology. Worcester: Clark University Press, 1934. P. 774. By permission of the publishers.)*

Notice, too, in Fig. 50, how visual acuity varies with the intensity of the illumination. At a low level, say, of −3 log millilamberts, visual acuity is only 0.1. This is the reciprocal of the visual angle in minutes of arc and thus is equivalent to about 10 minutes of arc. At extremely high levels of illumination, say, 3 log millilamberts, the visual acuity is nearly 1.8, which is about 30 seconds (½ minute) of arc. Visual acuity, then, gets much better with increasing illumination. This is a general principle which you will meet in almost all sensory functions.

Finally, in Fig. 50, you will see that two separate lines have been drawn through the points on the graph. These lines represent the duplicity of visual processes, of which we shall see more later. The short, slowly rising line at the bottom of the graph refers to the rod processes of the eye. From it you can see that the rods in the eye are extremely poor in visual acuity. The steeply rising line that covers most of the points in the graph refers to the cones of the eye. You can see that most visual acuity and especially good visual acuity depends on the cones of the eye. Later on, in the next chapter, when we go into the duplicity problem in more detail, you will be told how we know that these two sections of the visual acuity curve are in fact ascribable to the functioning of rods and cones.

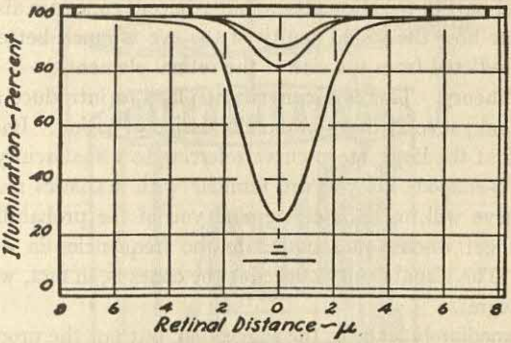

FIG. 51. The light distribution in the retinal images of three wires (see the lower part of the figure) computed in relation to the size of cones (see scale at top). (*From S. Hecht and E. U. Mintz. The visibility of single lines at various illuminations and the retinal basis of visual resolution, p.* 601. *J. gen. Physiol.*, 1939, 22, 593–612. *By permission of the Rockefeller Institute for Medical Research.*)

Minimum Visible Acuity. So far we have seen what visual acuity is, how good it is, how it depends on illumination, and how it goes along primarily with cone vision. Now let us ask how visual acuity is determined physiologically in the visual system. To answer the question we need no direct physiological experiments. We can simply take what we know of the structure of the retina and what we know about the actual visual image on the retina and put them together. For this purpose it is best to use minimum visible acuity, rather than minimum separable, for this gives us the best possible acuity measures and taxes the eye to the limit.

In a study using minimum visible acuity, measures of visual acuity were taken at several illuminations (Hecht and Mintz). The interesting fact is that visual acuity at the highest illuminations is, by this method, as little as 0.5 second of arc. This is especially interesting because we know from microscopic studies of the retina (Polyak) that the individual rod and cone elements of the retina are much larger than this. They are, in fact, on the order of 30 seconds of arc. How is it, we may ask, that the retina can discriminate 0.5 second arc when its smallest element is fifty or sixty times this size?

It turns out, when we examine the optic properties of the eye, that the actual pattern of the stimulus on the retina is many times the size of the visual object that can be seen. The eye is not by any means a perfect camera. Light going through it spreads out (diffracts) in the medium so that the image on the retina is a somewhat enlarged and distorted version of the original stimulus. By knowing the optical properties of the retina, it is possible to calculate the pattern that actually falls on the retina. This you can see in Fig. 51. What is a stimulus of 0.5 second outside the eye spreads out over a good many seconds of arc on the retina. In fact, it covers three or four cones. To be sure, one cone gets the greatest part of the stimulation, but adjacent cones are also stimulated. Thus we can see how the visual acuity of the eye is much better than might otherwise be predicted from the size of the retinal elements.

Probability Theory. This is a convenient place to introduce a notion that will come up again several times in our discussion of vision. Back in Fig. 50, you will note that the large, steep curve referring to visual acuity of the cones is sigmoid, or S-shaped. If you are familiar with statistics and probability theory, this curve will immediately remind you of the probability integral—the curve you get when you accumulate the frequencies in a normal bell-shaped curve. The visual acuity curve for the cones is, in fact, well fitted by a probability integral.

This fact immediately leads to the suggestion, but not the proof, of a theory of the physiological processes in the retina underlying visual acuity (Hecht, see Crozier). We might assume that the thresholds of the cones of the retina, at least at any given moment, are randomly distributed. Some are high, some are low, and some are in between, just as they would be in a normal bell-shaped curve. If this is true, then the number of elements that can be excited by the stimulus used in visual acuity will depend on illumination. The more intense the stimulus, the more chances of exciting the cones needed to give the visual acuity discrimination. And if the thresholds are normally distributed, the changes will increase with increasing illumination according to the probability integral. We could then explain the relation between visual acuity and illumination in terms of the random distribution of thresholds of the visual elements involved. We do not know at present whether this is the correct explanation, but it is feasible and it is a notion supported by prominent visual theorists (Hecht, Crozier).

Visual Acuity in Animals. So far we have been talking about visual acuity in human beings. Fortunately, however, we know a good deal about visual acuity in animals, too. In many animals, indeed, though not in all of them, visual acuity is an extremely easy thing to measure. To test it, we simply take advantage of the animals' natural reflex reactions to the movement of lines in their visual field. Some animals, such as certain fishes, strike at objects moving in the visual field. Some animals will swim, fly, or move toward the object. Others, especially the higher vertebrates, move their heads or their eyes in pursuit of moving lines. By arranging lines of different size, moving them slowly, and watching an animal's reflex reactions in an apparatus like that in Fig. 52, it is possible to tell whether it 'sees' them or not and thus to get a measure of its visual acuity (Smith).

Many animals have been tested by this technique: fishes, reptiles, birds, cats, guinea pigs, rabbits, and human beings (Warkentin). It is not of interest to us to consider the results in any detail. It is sufficient to note that there are no systematic differences in visual acuity in the vertebrate series. Some animals are slightly better than man, some slightly worse, depending upon minor differences in the structure and efficiency of their eyes.

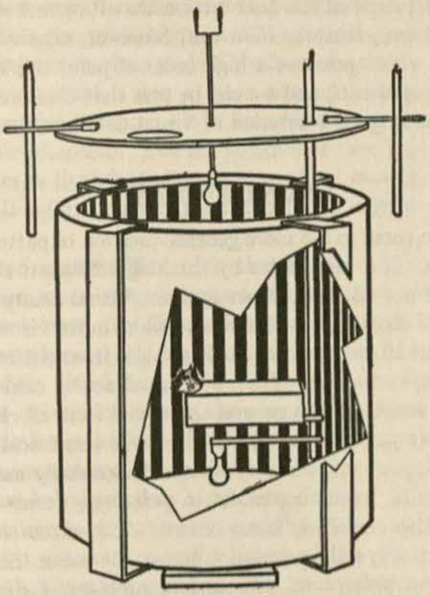

FIG. 52. Schematic side view of apparatus for the study of optokinetic reactions in animals. (*From K. U. Smith. The postoperative effects of removal of the striate cortex upon certain unlearned visually controlled reactions in the cat, p.* 145. *J. genet. Pyschol.*, 1937, 50, 137–156. *By permission of the Journal Press.*)

There is, however, one important point of interest in these animal tests of visual acuity. They let us study the role of central nervous structures in visual acuity (Smith and Warkentin). It is possible to remove experimentally the different parts of the visual system and determine the effect on visual acuity. So far, however, only the visual cortex has been studied in this respect, but it gives interesting results.

The important point is that the visual cortex is not at all necessary for visual acuity measured in this way (Smith *et al.*). If anything, the reflex reactions to moving stripes become somewhat more stable and dependable after removal of the visual cortex than in the normal animal. And when the stripes are reduced in size to the point at which the reactions disappear, thus giving us a threshold of visual acuity, it turns out that the visual acuity of the cat is just as good without the visual cortex as with it. We cannot conclude from these results that the animal can perceive objects just as well without the visual cortex as with it—we shall show in the next section that it cannot—for only a reflex reaction has been our measure. We can, however, conclude that the subcortical centers in vision preserve a high order of point-to-point projection in their synaptic arrangements, and we can be sure that these subcortical centers are capable of just as good resolution of visual detail as the cortical centers.

PATTERN VISION

It is now time to come to the more general question of pattern vision and its physiological basis. It is easy to see by thinking a moment that visual acuity is basic to most, if not all, pattern perception. Visual acuity is the ability to discriminate spatial distributions of dark and white in the visual field. Without any visual acuity at all, we could not tell triangles from circles or large objects from small objects, and so on. True, our visual acuity could be rather poor and we could still make out the general shape and form of visual objects, but in the end all pattern perception depends upon some visual acuity being present. On the other hand, good visual acuity does not necessarily mean good pattern perception. There is 'something more' to perceiving forms and sizes than simply telling whether one object is one or two. And, of course, ability to make a reflex reaction to, say, stripes does not necessarily mean the ability to make other types of form perception. There is a problem of discrimination and orientation involved in pattern vision that requires more than the basic visual acuity.

Pattern Vision and the Visual Cortex. There has been a considerable amount of research on the role of central nervous structures in pattern vision. Because most of this research comes out with the same answer, it is easy to summarize it rather briefly. Except for the reflex optokinetic reactions, it has been necessary to have trained subjects, either animal or human, for all the experiments. Human beings, of course, ordinarily acquire quite a repertoire of reactions to pattern so that they can easily identify such patterns as triangles, circles, squares, and so on. In animals, the reactions must be especially built up through training, although we can tell a good deal about the animal just from watching its behavior. The training, however, is just an instrument for finding out what the subject can see and cannot see. In the discussion here we do not have to pay any attention to the problem of learned and unlearned reactions. We will do that later in the chapter on discriminative learning.

In order that you will know where we are going, let us first make a flat statement about the physiological basis of pattern visions: *In mammals, pattern vision depends upon the visual area of the cortex and not upon any other structure of the nervous system.* This is the conclusion of all of the experiments on this subject. We will now summarize the evidence on which it is based.

The primary receptive area for vision in the cerebral cortex is variously known as the visual area, the visual cortex, the striate cortex, or Brodmann's area 17. It receives the projections from the lateral geniculate body of the thalamus, which in turn receives projections from the retina. When the visual area is removed from a cat, a dog, a rat, a monkey (Klüver)—and quite certainly also chimpanzee and man—it is immediately obvious that something has happened to detail vision. The subject cannot "see" his way around. He bumps into objects as though he did not know they were there. In a word, it looks as though all ability to see objects or patterns is gone—as though visual acuity is zero.

Systematic experiments confirm this observation. Animals can be given simple patterns like triangles and circles to discriminate. Without the visual cortex, they cannot learn the discrimination. Human beings can be given similar problems or they can be asked to tell the position of any visual object or bright patch in their visual field. They cannot do it. By any visual test, therefore, animals or humans lacking the visual cortex have no visual acuity, no ability to discriminate the form of objects. Animals can, as we just pointed out, make reflex movements of the head or eyes to moving stripes in their visual field, but this must be regarded as a reflex mechanism of subcortical centers. It is not pattern vision in any other sense of the word.

It is well to point out that in partial lesions of the visual cortex in various mammalian animals, there is a corresponding loss of detail vision in a part of the visual field (Ranson, Nielson). This fact is easily demonstrated in human individuals who have suffered wounds in part of the visual areas. In such individuals one can find *scotomata*—regions in which objects cannot be seen or identified in the visual field by a simple mapping procedure. A small object is presented first at one place in the visual field and then at another and the subject is asked to say whether or not he sees it. By fully exploring the visual field in this fashion, one can plot the region of scotoma. The region, when it is found, can be predicted with reasonable accuracy by knowing that there is a point-to-point projection of the retina on the visual cortex.

Spatial Vision. Although many experiments have been done with pattern vision and the visual cortex, few have carried the analysis further to see what other aspects of spatial vision are disturbed in 'cortical blindness.' One investigator, however, has made a careful study of the monkey after ablation of the visual cortex (Klüvér). In addition to the loss of pattern vision, Klüver finds, the monkey is also lacking in all other spatial aspects of visual function.

To find, as he did, that such monkeys cannot make any discriminations of depth or distance is not unexpected. Not so predictable, however, is the fact that the cortically blind monkey cannot distinguish the size of objects either. Actually, if two stimulus patches of different size and of similar brightness are put before the monkey, it can, after sufficient training, come to distinguish the two patches. Appropriate controls, however, show that what the monkey is discriminating is the total amount of light given off by each of two patches rather than their size, for when the intensity of the two lights is made to match and their sizes are different, the discrimination breaks down.

The matter of intensity vision and the visual cortex will be pursued further in the next chapter. Here we should note that no spatial vision, whether of pattern, form, distance, or size is left when the visual cortex is removed. Because all the animals studied have given comparable results when subjected to the same experimental conditions, it is fair to say that this conclusion applies to the gamut of mammalian animals from the rat to man.

These statements, however, do not apply to inframammalian animals. And the reason is a good one. They do not have a neocortex worth the name (see Chap. III). In the bird, for example, there is a thin layer of cells in the occipital region, as in the rest of the cortex, representing the beginnings of the cerebral cortex seen more highly developed in the mammals. This cortex, however, seems to have no significant function. At least, the removal of the cortical tissue does not have any effect on visual functions that can be detected by any of the usual tests in animals (Layman). Apparently, then, in birds and in the lower animals all functions of pattern and spatial vision are conducted at a subcortical level. Moreover, it follows that when some visual functions are transferred in the course of corticalization of function to the cortex, these functions are the spatial functions in vision—not, as we shall see later, the brightness functions.

Autonomy of the Visual Cortex. We have been saying a lot about the importance of the visual cortex in pattern vision. Perhaps it would be well to say also what other areas of the visual cortex do not do. In human subjects, there is no evidence that any other area of the cortex than the visual area 17 is important in the primary capacity to see patterns. Other regions certainly have something to do with complex processes of recognizing the meaning of visual objects and symbols, but not with the 'seeing' of them. Whenever the question has been tested in animals, the story has been the same. Lesions outside of the visual area do not impair pattern vision (Lashley). There is one exception to this statement, in which rats were tested for their ability to discriminate an upright F from an inverted F (Kirk). Rats with severe lesions, apparently outside the cortex, seemed to have some difficulty learning the discrimination. There is reason to believe, however, that the lesions in these cases invaded the projections from the geniculate body to the cortex and thus interfered with the visual cortex (Lashley). For this reason and because his own extensive experiments on the question yielded negative results, Lashley concludes that the visual cortex is completely autonomous in its pattern-vision functions. It, and no other area, is responsible for spatial vision.

MOVEMENT VISION

There is one more aspect of vision which properly falls under the heading of spatial vision yet has temporal properties as well. This is the visual perception of movement. Movement involves a spatial distribution of light on the retina, but a distribution that changes in one direction or the other in time. This temporal character of movement makes it a little different from the other spatial aspects of vision that we have been discussing. At any rate, the physiological basis of movement vision is somewhat different from that for other aspects of spatial vision.

There are two kinds of movement to consider. One is real movement, in which some object moves continuously on the retina. The other is apparent movement, in which there is no object movement but there appears to be such movement. We have relatively little physiological research on either of these kinds of movement, but such as we have we will discuss. There is no direct physiological research on apparent movement, but there are some interesting psychological experiments from which some inferences about physiological processes can be made. We have a little work on the role of the visual cortex in real movement perception. We shall take up these topics in order.

Kinds of Apparent Movement. There are three basic types of apparent movement that have been described. The first is *beta* movement. If two disks of light are presented briefly and in succession to different parts of the retina, movement tends to appear in the direction of succession. This is the common variety of apparent movement now so popular in advertising signs. Whether the movement seen is good movement or jerky and incomplete depends upon three principal aspects of the stimulus situation (Korte's laws): the size and intensity of the stimuli, the distance separating them, and the interval of time between their presentations. The greater the spatial separation or the temporal interval, the greater must be the intensity; and the impairment of optimal movement caused by changing one of these factors can, within certain limits, be offset by altering either of the others.

The second type of apparent movement is *delta* movement. This is essentially the reverse of beta movement. Sometimes in a situation that would otherwise produce beta movement, if the second of two flashes is much brighter than the first, movement backward from the second to the first flash will be seen.

The third type of apparent movement is *gamma* movement. This is a movement of expansion or contraction. When a disk of light comes on suddenly, its center seems to appear first and then to expand, filling out the disk. Likewise, when the light goes off, one's experience is of a contraction of the light to its center, where it vanishes.

Physiological Explanation. At present, our attempt to understand the physiological mechanism of apparent movement rests on some facts of physiological function of the retina, some experiments with visual factors affecting apparent movement, and a few assumptions. The experiments were carried out by Bartley and are illustrated in Fig. 53. They were tests of the kinds of movement seen by observers when given a number of different stimuli. In Fig. 53, you see them diagrammed. The dotted lines represent the visual stimuli. The solid lines represent the spatial distribution of light on the retina, calculated by making allowances for diffraction and stray light in the retina. The arrows indicate the direction of apparent movement seen by the observer, and the length of the arrow indicates roughly the relative 'strength' of the movement experienced. We will come back to these experiments in a moment.

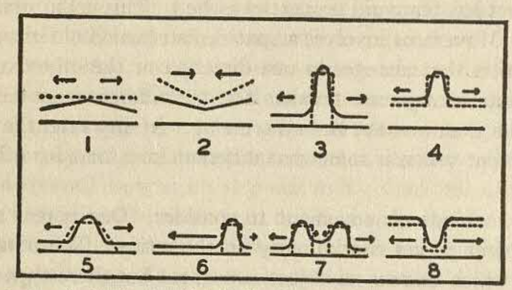

FIG. 53. Eight cases of visual stimuli and the direction of apparent movement which they produce when the stimuli have a sudden onset (as determined in experiments by Bartley). The bottom line in each case is merely a base line. The dotted lines represent the distribution of light in the stimulus. The solid line represents the distribution of light on the retina; this is somewhat different from that of the stimulus outside the eye because of the optical properties of the eye. The arrows indicate the direction in which apparent movement is seen, and the length of the lines represents roughly the relative magnitude of the apparent movement. The cases illustrate the fact that apparent movement under the conditions indicated depends in part on the gradient of illumination in the retinal image and in part on the different behavior of the center and periphery of the retina. (*From S. H. Bartley. The relation of retinal illumination to the experience of movement, p.* 476. *J. exp. Psychol.*, 1936, 19, 475–485. *By permission of the publishers.*)

It is not possible to have every physiological fact in hand just at the time one needs it. Several of the facts about retinal physiology that we need to understand apparent movement will not be taken up until the next chapter. In lieu of these facts, we must ask you at the moment to accept some statements on faith. (1) Receptors in the center of the retina respond to stimulation more quickly than do those in the periphery. (2) The more intense the stimulus the more rapidly is a receptor excited. This one might expect by common-sense reasoning, but it is upheld too by direct physiological measurements. (3)

There is a spatial interaction in the retina which, under the appropriate conditions, causes some facilitation [1] of neurons in areas adjacent to a stimulus but not directly affected by the stimulus. This is the kind of spread one expects from the divergence of synaptic connections in the retina, including the lateral neuron connections. (4) Illumination of a limited area of the retina will, as we have already seen, spill some light into other areas of the retina through stray light and diffraction in the media of the eye.

Gamma Movement. Two of these factors, the greater sensitivity of the center of the retina and the straying of light, are probably of basic importance in explaining gamma movement—the expansion and contraction movement. Item 1 in Fig. 53 is an example of gamma movement when the whole eye is illuminated. Through diffraction and straying of light, more light is concentrated in the center of the eye than at the periphery, making for shorter latency in the center than in the periphery. This alone would produce the expansion and contraction. In addition, however, the greater sensitivity of central receptors also contributes the movement, as is illustrated in items 3 and 4, where the stimulus was restricted to the central portion of the eye. This is further supported by item 6, in which the spot was presented off the center of the eye and greater movement was seen in the direction of the center than away from it. On the other hand, the factor of greater intensity also plays an important role, for Bartley was able to reverse the usual gamma movement (see item 2) simply by making the outside of the stimulus patch a little more intense than the center. In this case the patch contracted at onset and expanded when it went off—the opposite of the usual gamma movement.

Beta Movement. Turning now to the problem of beta movement, similar factors apply, but the spatial interaction of the retina must be especially emphasized—or at least spatial interaction in the visual system. The effects of stimulation of two retinal areas do summate, we know (see Granit), if the areas are not too far apart on the retina or too separated in time of stimulation. The spatial summation must occur either through the activity of lateral neurons in the retina or through overlapping of synaptic endings at all levels of the visual pathways. We are certain that the retina plays some part in this interaction, but the brain is probably involved in it too. Consequently, beta movement may be regarded as equivalent to real movement in that there are neural excitations aroused successively in the stimulated areas in both cases.

Delta Movement. This, finally, can be readily understood in terms of the greater speed of reaction of receptors subjected to high intensities of stimulation. This difference in latency of response is apparently so great that, although one light may appear after the other, its greater intensity causes the cells stimulated by it to give a burst of impulses before the cells exposed to the weaker light.

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[1] Facilitation, as used here, means that stimulating one part of the retina can change the threshold, or make excitation easier, in an adjacent part.

'Subcortical Apparent Movement.' We shall go on now to the higher centers of the visual system in visual movement. You will remember that earlier in this chapter we described the reflex reactions of animals to moving stripes in the visual field. This same situation can be used to study a type of apparent movement in animals (Smith). All one has to do is to illuminate the moving striations with an intermittent stimulus so that the stripes are seen only momentarily in successive positions. This is the essential feature of apparent movement.

Cats respond to such a stimulus field with optokinetic reactions. Their eyes follow the 'moving' stripes just as they do stripes that are really moving. Moreover—and this is the interesting point from a physiological point of view—removal of the visual cortex does not impair this reaction to apparent movement, just as it has no effect on similar real movement. Apparent movement of a sort, therefore, can be carried out by subcortical centers in the absence of the visual cortex. To be sure, we know nothing of the 'conscious' experience of the animal, but the reflex behavior gives every indication that the essential neural processes for apparent movement do not require the cortex. This fact might indicate, although it does not prove, that these processes normally originate in the retina or in the subcortical visual centers. At any rate, it seems that certain aspects of apparent movement can be understood at this level of the visual system.

Real Movement and the Visual Cortex. We come finally to the question of cortical functions in real movement. We have only two experiments on this question, both on cats. In one experiment, the animals were trained to distinguish between a stationary spot and a spot moving in a circle (Kennedy). In the other, the cats had to discriminate between two sets of stripes, one moving and the other stationary (Morgan). Neither of the experiments were particularly thorough or satisfactory. They both demonstrated that cats without the visual cortex can discriminate real movement. They agreed, however, in finding that the rate of movement required for such discrimination was considerably higher after cortical 'blindness' than before. Moreover, the performance of the animals was so unstable as to prevent measurement of postoperative thresholds. Thus it is clear that movement perception is radically impaired without the visual cortex, but it is not abolished.

This conclusion, however, should be tempered with a word of caution. It is sometimes hard to know what an animal is discriminating, and it is entirely possible that the cats, postoperatively, were not really discriminating movement in the spatial sense of the word. We noted in introducing the discussion of movement that it has both a spatial and a temporal aspect. The temporal aspect of the moving stimulus alone is an alternation of dark and light stimuli on any given spot of the retina, much as one gets in a flicker discrimination. We shall come to flicker in the next chapter, where we shall see that flicker discrimination, like intensity discrimination, is relatively intact without the visual cortex. It is possible that the cats in the movement experiments were not discriminating movement at all in the true sense of the word but something that might better be called flicker discrimination.

ANATOMICAL DETERMINANTS OF SPACE PERCEPTION

We have seen that, in mammals, reflex reactions to visual details may be mediated by subcortical centers, but space perception depends on the visual cortex. We have seen, too, that both the visual cortex and the superior colliculus of the midbrain are arranged anatomically so that they preserve a point-to-point projection of the images falling on the retina. This anatomical arrangement provides the essential mechanism for spatial vision. Although spatial organization of the visual system may be necessary for spatial vision, visual scientists have long been asking whether it determines the characteristics of spatial perception.

Psychological Approaches. This question has several forms. One is to ask whether our perception of space is inherent in the arrangement of the nervous system or whether it is acquired through experience. Many experiments have been carried out to answer this kind of question. In man, there have been several attempts to see what happens when people wear glasses that turn their visual field around or upside down (Stratton, Ewert). These experiments are not entirely consistent, but they show that man does not readily adjust to such a drastic reorientation of his visual field. In the chimpanzee, the experimental method has been to bring chimpanzees up in the dark from infancy until they are well along in their development (Riesen). In this case, when the animals are brought into the light they are completely disoriented and act as though they must learn slowly the correct way to see spatial relationships. In the rat reared in darkness, on the other hand, no experience seems to be necessary (Lashley and Russell). The rats can jump in the correct direction and to the correct distance of an object when they are first brought into the light.

Physiological Approaches. All these experiments are interesting, but they do not address the problem in physiological terms. Deserving more attention here are some experiments that use physiological methods to assess the role of the anatomical organization of the visual system in space perception (Sperry, Stone). All the experiments have been done in amphibian animals, such as the frog, the newt, and the toad, because it is only in these animals that the operative technique works well. This technique is to cut the optic nerve, remove the eye, replace it in a different orientation and observe the effects on the animal's reactions to visual space.

Specificity of Organization. Several different experiments have been carried out, all showing the same thing. In the simplest experiment, the optic nerve is completely severed without changing the position of the eyeball. In due time the nerve regenerates, and the animals show by their reaction to moving objects or to food lures that they can see again. And the interesting point is that their space perception returns to practically normal performance. By their localization of objects and their following of objects with their head and eyes, it is clear that they have good spatial vision. This means that the optic nerve reestablished the proper spatial organization when its fibers grew back to the thalamus and midbrain.

A second important point can be demonstrated with several variations of technique. At the same time that the optic nerve is cut, the eye can be rotated in its socket 180 deg. This, of course, means that an object stimulates the side of the retina opposite from what it did before. It is also possible to transplant the eye from the left socket to the right one, or vice versa, at the time the optic nerve is severed. Depending on how the eye is oriented in its new position, this change will reverse either the up and down or the right and left, not both. When the optic nerve regenerates and vision is restored, we have a chance to see what these drastic changes do to vision.

Without going into all the details of the results, let us make the main point clear. The optic fibers grow back to exactly the same anatomical arrangement that they formed before the operation (Sperry). The rotation of the eye and the severing of the nerves do not alter the point of termination of the respective fibers from the retina. This is clear in the behavior of the animal. When it is shown an object in its left visual field, it jumps to the right. When shown one in the upper visual field, it jumps down. Similar reactions occur with moving stimuli. In every case the behavior indicates that the fibers grew back to the quadrants in the brain to which they originally connected.

You can imagine how maladaptive these reactions to visual space must be in cases of transplanted or rotated eyes, and you might think that, in time, the animal would learn to readjust itself to the change. But it does not. Animals kept for long periods of time after restoration of vision continue to show maladaptive reactions, jumping or moving their heads in the direction away from the visual stimulus, rather than toward it.

It would be foolish to take these results with amphibians and jump to conclusions about man. Nevertheless, they show clearly that in the amphibian there is some kind of specificity of the nerve fibers and their centers in the brain which sees to it that their connections are formed in a 'prearranged' plan—that one part of the retina is connected with a corresponding part of the central center, no matter how maladaptive that may be. In the amphibian, moreover, the results show that the anatomical arrangement of the visual system, not learning, determines the kind of space perception that will take place.

This phenomenon of specificity of fiber connections is an important fact in understanding the physiological mechanisms of behavior—even if it is still something of a mystery. We shall meet it again and consider it in more detail later in connection with the establishment of reflex patterns of behavior.

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CHAPTER VIII

BRIGHTNESS VISION

When used correctly, the term *brightness* refers to the psychological experience of intensity (Chapanis). It does not mean the physical intensity of a visual stimulus. To be sure, experienced brightness depends in part on physical intensity, but it also depends on the wave length, the time of stimulation, the state of adaptation of the eye, and several other minor factors. Moreover, in discussing the topic of brightness, we must include not only the data of differential brightness discrimination but also the facts of minimum brightness, *i.e.*, the absolute intensity threshold in vision. In this chapter, therefore, we shall consider both absolute and differential brightness sensitivity as they are affected by various parameters of time, wave length, and adaptation. We shall attempt to bring together present knowledge of the physiological mechanisms that underlie the relations of these various factors to brightness vision.

VISUAL PHYSIOLOGY

There is a tremendous amount of experimental information available in the field of brightness vision, and we shall be able to cover only a part of it. Our information comes from various sources—photochemistry, histology, electrophysiology, and psychophysics. We shall try to tie these various aspects of vision together. The relationships, however, are often quite complicated, and it is necessary to have a general background in visual physiology to understand them easily. In this first section, therefore, before we tackle the primary problems of brightness vision, we must take a little time to run over our basic knowledge of the physiology of visual processes.

The Duplicity Theory. This theory is one of the most firmly established of all principles in vision—perhaps too firmly established. It was put forth by von Kries at the end of the nineteenth century and has gathered more and more support as our knowledge of visual functions has increased. As we shall see, especially in the next chapter, modern physiological knowledge is beginning to raise many questions about it and to force revisions in our thinking about it. But before we get into those, let us discuss what the theory is and how it is supported.

The fact that there are rods and cones, two usually distinct kinds of receptors, in the eye is the basic point of the duplicity theory. These two types of receptors are regarded as making up two systems in vision, each with its own properties. The rods are for night vision at low illuminations; they are much more sensitive than the cones and can be used when there is very little light. The cones are the daylight receptors, operating when illumination is high. The cones can see color; the rods, only shades of black and white. The rods are most sensitive in the greenish part of the spectrum; the cones are most sensitive in the yellowish part of the spectrum. The cones are most numerous in the central part of the eye, their connections with neurons of the visual system are more point-to-point, and the cones thus are most involved in space perception and visual acuity. The rods, on the other hand, are more numerous in the periphery of the eye, great numbers of rods converge on a small number of ganglion cells of the retina, and the rods thus are specialized, not for spatial vision but for intensity vision and for sensitivity to very weak stimuli.

All these statements are part of the general statement of the duplicity theory. You will find, as we go along, that they are not all true, at least not all strictly true. But as matters stand today, this general statement of the dual system in the eyes of animals and man is a good approximation, a good rule of thumb to go by in thinking about vision. So you should keep it in mind.

Photochemistry. Knowing that the eye is a photosensitive camera and that nervous processes are electrochemical, you would certainly not be surprised to learn that vision begins with a photochemical process. Kühne and Boll discovered that nearly seventy-five years ago, and we now have abundant evidence from the researches of biochemists. In fact, some of the photochemical substances that are involved have been extracted from the retina and have been made to break down and regenerate in test-tube experiments outside of the retina. By such experiments the intricate chemical processes involved in the stimulation of the eye by light have been learned step by step. We will not take you into all the steps by which the present knowledge has been achieved but will simply present matters as they stand today.

Visual Purple. It was in the rods of the eye that a photochemical substance was first discovered. You might expect that, because, as we said above, the rods are much more sensitive to light than the cones and thus ought to have much larger quantities of their photochemical substance. This has been called *visual purple* or *rhodopsin*.[1] This substance can be extracted and studied in the test tube. There it will undergo breakdown in a very systematic manner when exposed to light. The rule for its breakdown is a simple one: it decomposes in proportion to the intensity of the light and the quantity of visual purple present. This decomposition is brought about, as you might expect, because visual purple absorbs a large percentage of the light falling on it. In fact, the amount of decomposition is directly proportional to the amount of light absorbed.

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[1] There are certain fishes that have visual violet in their rods rather than visual purple. For further information about them see Wald, 1937.

That brings us to the property of visual purple that is most interesting from the point of view of brightness vision: its spectral absorption curve. This you can see in Fig. 54 as the relative amount of light absorbed by the material at different wave lengths. As you can see, visual purple is most effective in absorbing light at a wave length of about 510 mμ.[1] On either side of this maximum, absorption falls off gradually till it becomes negligible above 600 mμ and in the region below 400 mμ. Later on we shall compare this curve with some of the properties of human vision.

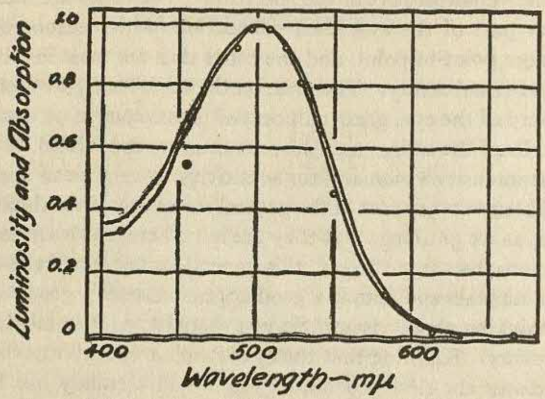

FIG. 54. Comparison of the scotopic visibility curve (points) with the spectral absorption curve of visual purple (lines). (*From S. Hecht, S. Shlaer, and M. H. Pirenne. Energy, quanta, and vision, p. 831. J. gen. Physiol., 1942, 25, 819–840. By permission of the Rockefeller Institute for Medical Research.*)

Decomposition Products. We know now that visual purple goes through at least three different steps in its decomposition (see Chapanis). These can be seen in the diagram of Fig. 55. The first step is *transient orange*, so called because the product is both orange and very transient. Depending somewhat on the acidity of the solution and on the temperature, transient orange breaks down more or less rapidly into the seond stage of decomposition, *visual yellow* (also sometimes called indicator yellow or retinene). This stage is much more stable and is clear enough to be seen in almost all experiments with visual-purple breakdown. The final stage of decomposition, resulting from the further decomposition of visual yellow, is called *visual white.* This you see on the bottom right of Fig. 55. We might point out in passing that these substances are named because of their respective absorption characteristics. Visual purple absorbs green and yellow, reflects blue and red; transient orange absorbs blue and green, reflects yellow and red; visual yellow absorbs blue, reflects green, yellow, and red; and visual white reflects everything in the visible spectrum.

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[1] This measure (mμ) is millimicrons, meaning one-thousandth of a micron. A micron is one millionth of a meter or one thousandth of a millimeter. A millimicron is equivalent to 10 angstroms—units used frequently by physicists. Some would prefer that we talk about light in terms of frequency, but it has become the custom to specify it in terms of wave length, as we do here.

Regeneration. Although visual purple is decomposed by light very easily in the test tube, it does not so easily regenerate. Actually, if the chemical conditions are right, some regeneration (15 per cent) can be obtained in extracts (Hecht *et al.*), but much better results are obtained in living or excised eyes (Peskin). But various combinations of experiments can be and have been done, and some points about regeneration now seem clear. As you see in the diagram, there are two points at which regeneration can take place. One is regeneration back directly from transient orange, the first breakdown product. All indications are that this is a relatively fast process. The other type of regeneration is from visual white, the last breakdown product. This process is certainly much slower than that from transient orange. Moreover, it involves new substances and new materials supplied by the blood and tissues surrounding the retina.

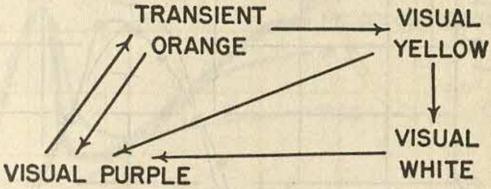

FIG. 55. Simplified scheme of the photochemistry of the retina. Visual purple when hit by light waves breaks down into transient orange and this, being unstable, either goes back quickly to visual purple or breaks down further to visual yellow. This may regenerate visual purple, either directly or indirectly via an intermediate product, visual white. The different routes for rebuilding visual purple have different speeds, and that from visual white is the slowest.

Cone Substances. Having found a photosensitive substance in the rods of the eye, biochemists naturally have been looking for corresponding substances in the cones. All early attempts (before 1900), however, to find such substances failed. The first claim of its discovery was made in 1937 (von Studnitz), and shortly thereafter several others also brought forth data apparently pointing to a cone substance (Hosoya *et al.*, Chase, Hanström, Wald). Unfortunately, however, there was relatively little agreement between these various reports. Some workers reported three different cone substances; others reported only one each, but one that was different in absorption characteristics from that reported by another investigator. The result is that most of the work at the present time is rather untrustworthy (see Granit or Bliss). That is to be expected, however, in view of the unavoidable difficulties of experimentation.

There does, however, seem to be one cone substance in which we can have some faith. This has been called *iodopsin.* It has been prepared by Wald and by Bliss. To detect the substance and determine its absorption spectrum, a special technique is necessary. The retina is extracted as it would be for rhodopsin. Then its absorption spectrum is measured. Next the extract is bleached with red light (615 mμ), which has relatively little effect upon visual purple but should bleach out the cone substance rather rapidly (see page 178). Then the absorption curve is taken again. The difference between the curve taken before bleaching with red light and afterward should be the curve of the cone substance. In Fig. 56, curve *B*, you see that this curve has a maximum at about 560 mμ. Later the remaining extract is bleached with white light and the difference in absorption spectrum again calculated. This curve, also shown in Fig. 56, is, as you might expect, the curve for visual purple.

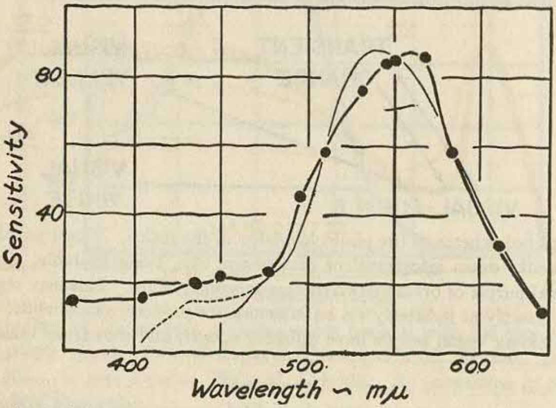

FIG. 56. The absorption spectrum of the cone substance, iodopsin, and the photopic luminosity curve (*cf.* Fig. 54). The light line is the spectral sensitivity of the human eye at high levels of illumination (the dotted line is a small correction of this curve), and the heavy line through the dots is the spectrum obtained from extracts of the retina prepared in the way described in the text. (*From A. F. Bliss. The chemistry of daylight vision, p.* 290. *J. gen. Physiol.,* 1946, *29,* 277–297. *By permission of the Rockefeller Institute for Medical Research.*)

It looks, therefore, as though we can be sure of the existence of a substance in the cones that is different than the visual purple of the rods. That is the best assumption to go on at present. There are, however, reasons for caution. (1) Even though this substance may be demonstrated, we cannot be sure that it actually came from the cones. For in extraction, whole retinas, rods, cones, and other cells as well contribute to the extract. (2) Even though the substance is photosensitive, we do not know certainly whether it is the substance involved in visual processes. It is perfectly possible for a photosensitive substance to exist without entering into the processes of vision of the eye. (3)

The substance iodopsin may not be just one substance; it may be several substances which happen to yield to the same extraction procedures. It is quite possible that with appropriate techniques this substance might be fractionated into more than one substance. These are all possibilities which can be tested only when the appropriate techniques and further research give us clear answers.

The Electroretinogram. The physiology of the retina has been studied in terms not only of its chemical processes but also of its electrical activities. These are best recorded by placing one electrode upon the cornea and another at the back of the eye. From such electrode placements one picks up the electrical changes occurring in the retina when it is stimulated by light (Granit).

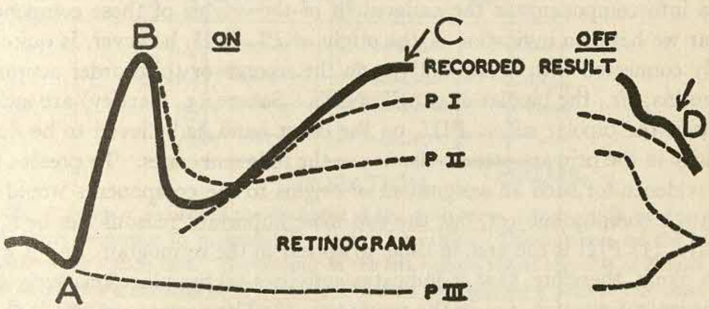

FIG. 57. The electroretinogram and its analysis into components as suggested by Granit. *A* is the first positive wave and *B* the first negative wave. Following this is a slow negative *C* wave and a wave *D* in the positive direction when the stimulus goes off. The three components are *P*I, *P*II, and *P*III, and it is their mixture in various ways that is presumed to make up the various waves of the record. (*From S. H. Bartley. Some factors in brightness discrimination, p.* 347. *Psychol. Rev.,* 1939, **46,** 337–358. *By permission of the American Psychological Association.*)

These changes are as follows (Fig. 57): First, when a light is flashed on, there is a slight negative electrical change (*A* wave), but this is followed shortly by a substantial positive change (*B* wave) and then by a reduced and longer persisting positive wave (*C* wave). If now the light is turned off, there is a slight positive hump (*D* wave) and then a slow return to neutrality. These are the typical electrical effects seen in visual stimulation. They vary considerably, however, with the intensity and duration of the stimulus. With weak light the *A* wave may not be present, and with very short flashes none but the *A* and *B* waves may be seen. Both the *latency* and the *height* of the *B* wave, on the other hand, vary with the intensity of light, and this fact has been used to measure the effectiveness of visual stimulation (Graham and Riggs).

Analysis of Retinogram. The electroretinogram, just described, must be regarded as the composite of several different electrical effects. As yet no completely satisfactory analysis of its components has been given, although that of Granit seems most adequate and probably approximates the 'truth.'

After performing experiments in which various changes in the electroretinogram were found in different species of animals or were induced by the use of drugs or anesthetics, he proposed that the retinogram be regarded as made up of three components, called *P*I, *P*II, and *P*III, respectively. *P*I is a slow, prolonged positive wave accounting for most of the *C* deflection; *P*II is the more abrupt and short-lived positive deflection seen in the *B* wave; and *P*III is a small negative deflection responsible for the *A* wave. The off-effect (*D* wave) is to be ascribed to a combination of changes in the three components.

Origins of Components. Even more problematical than analyzing the retinogram into components is the assignment of the origins of these components. So far we have no indication of the origin of *P*I. *P*II, however, is quite certainly connected with neural activity in the second- or third-order neurons of the retina, *viz.*, the bipolar or ganglion cells. Some (*e.g.*, Bartley) are inclined to favor the bipolar cells. *P*III, on the other hand, is believed to be due to activity in the primary sense cells, *i.e.*, in the rods and cones. To present fully the evidence for such an assignment of origins to the components would lead us into a complex subject, but the two most important reasons can be stated briefly. (1) *P*III is the *first*, in time, to appear in the retinogram, and it would seem likely, therefore, that it indicates activities taking place relatively early in the retinal reaction, *i.e.*, in the receptors. (2) The presence of *P*II is closely associated with the appearance of nervous impulses recorded in the optic nerve, a fact relating *P*II to retinal processes farther 'downstream' than the initial excitation. *P*II, furthermore, is blocked by anesthetics and drugs that depress nervous activity, while *P*III may still be obtained. For these reasons we ascribe *P*III, tentatively at least, to the sense cells and *P*II to neural effects farther on, probably in the bipolar cells.

THE PHYSIOLOGY OF CENTRAL VISUAL MECHANISMS

The Optic-nerve Discharge. One can record electrical activity from the optic nerve in much the same manner as it is picked up from the retina. The form of the optic-nerve response is quite different, however, from that of the retinogram and is dependent both upon the kind of animal and the conditions of stimulation employed (see Fig. 58). In the frog one can distinguish three distinct peaks in the recorded action potential when the time of light stimulation is not too brief (Bishop). First comes a large wave and then close upon it another nearly as large; much later there is a small wave rising and falling more slowly than either of the first two. (The third wave, however, is probably not present in mammals.) This pattern, the reader will see in a later chapter, is very much like the action potential of a cutaneous nerve. It appears to indicate three different groups of fibers of different sizes and different rates of conduction. From the largest to the smallest, they have been called *A*, *B*, and *C* fibers when considered in cutaneous nerves, and there they are associated with different sensory functions.[1] Such is probably also the case in the optic nerve.

In the rabbit, no *C* waves but only the *A* and *B* waves are observed in the optic-nerve potential (Bishop, see Fig. 58). In addition to these two waves, a third appears when the stimulating light is turned off, and it is accordingly called an *off-response.* This is interesting, because it indicates that some ganglion-cell fibers have fired in response to the *cessation of light.* No doubt is left about that fact when the technique of recording is so refined as to give the action potential of individual ganglion cells (Hartline, Fig. 59). We find, then, that there are three distinct types of fibers in the optic nerve. (1) The *X* type, which gives a burst of impulses at the beginning of stimulation and

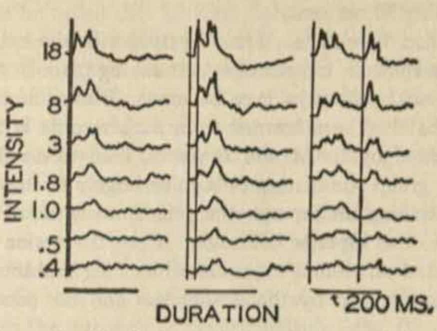

FIG. 58. A group of records of the discharge of the optic nerve. Each group, reading downward, shows responses to progressively weaker intensities. The numbers on the left are 10^3 candles per square foot. The column on the left is for a visual stimulus of 8 msec., that in the middle for a stimulus of 30 msec., and that on the right for a flash of 135 msec. The time line is 200 msec. Note the off-response showing up clearly when the flash is 135 msec. Also note the two distinct parts of the on-response in the records taken with strong stimuli. (*From S. H. Bartley and G. H. Bishop. Optic nerve response to retinal stimulation in the rabbit, p. 39. Proc. Soc. exp. Biol. Med.*, 1940, **44**, 39–41. *By permission of the publishers.*)

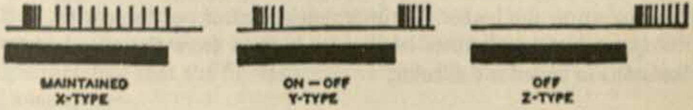

FIG. 59. Diagram of the activity of three types of ganglion cells distinguished in the vertebrate eye by Hartline. (*From S. H. Bartley. Some factors in brightness discrimination, p. 340. Psychol. Rev.*, 1939, **46**, 337–358. *By permission of the American Psychological Association.*)

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[1] It is not customary to designate the three waves of the frog's optic-nerve potential as *A*, *B*, and *C*, respectively, nor the two waves of the mammalian potential as *A* and *B*. Since, however, the parallel has been suggested (Bishop and Heinbecker) and since so naming them makes it much easier to refer to them, the practice has been adopted in this and the following chapter.

settles down to a steady rate of discharge during illumination, constitutes about 20 per cent of the total number of ganglion cells. (2) The *Y* type, which fires only at the beginning of stimulation and at its end, makes up about 50 per cent of the total. (3) The *Z* type, which responds only when light is turned off, constitutes the other 30 per cent.

Subcortical Action Potentials. From electrodes in the external geniculate bodies or superior colliculi, records of events taking place in these subcortical stations of the visual pathways may be made (Bishop and Bartley). One important fact that has been learned from such records is that two sets of impulses, represented by the *A* and *B* waves, tend to divide at the lateral geniculate, the *A* group stimulating cells going largely to the optic cortex and the *B* group continuing on through the geniculate without making synapse and proceeding to the superior colliculus. Here the action potential arises mostly from *B* impulses, although in some animals (*e.g.*, rabbits) two elevations may be seen, one initiated by the *A* impulses and the other due to the *B* impulses.

Response of the Optic Cortex. The optic cortex, on the other hand, though usually affected by both sets of impulses, is activated more easily and to a greater extent by the *A* group of fibers. This fact suggests that only a small proportion of the ganglion cells of the retina affect the optic cortex, since the *A* group of fibers makes up only about 20 per cent of the total of ganglion cells.

When the retina is stimulated by light, or the optic nerve by an electric shock, electrical activity appears in the cortex, but in a complex fashion which cannot be represented by a simple diagram. By placing the electrodes at different layers of the cortex, however, and observing the character of the changes in the cortical potential, a partial analysis of this cortical activity has been made (Bishop and O'Leary). It appears that at least three groups of cells make successive contributions to the potential: (1) fibers of the optic radiation leading up to the cortex, (2) internuncial neurons of the cortex, and (3) corticofugal (or efferent) fibers leading back down from the visual cortex to the thalamus or superior colliculus.

PHYSIOLOGICAL THEORIES OF BRIGHTNESS VISION

You now have the rough outline of our present knowledge of photochemical and electrical events underlying vision. As we go along in this chapter and the next, we shall introduce additional physiological details where they are relevant to the problem under discussion. In the meantime, however, you ought to have a brief glimpse of some of the theoretical work that has been done in an attempt to explain brightness vision in theoretical terms. Many people have proposed theories to explain various individual aspects of brightness vision, but all of them belong primarily to one or the other of two camps, the photochemical theory and the statistical theory. Each of these has been extensively developed in a mathematical form.

Photochemical Theory. The late Hecht was the scientist most responsible for a full treatment of brightness vision in terms of photochemistry. The principles of his theory were simple. He assumed that there were three basic chemical reactions taking place in each of the primary photoreceptors of the eye. One reaction he called the "primary light reaction"; this was the breakdown of visual purple or photochemical substance by light. A second was the "primary dark reaction"; this was the regeneration of the photosensitive substance from its breakdown products. The third reaction was the "secondary dark reaction"; this was a chemical process resulting from the breakdown of photosensitive substance which in some way or other brought about the nervous impulses and transmission necessary for vision.

On the basis of known facts of photochemistry outside of the retina, such as that taking place in a photographic plate, Hecht could make certain assumptions about the course of each of these supposed retinal reactions. He could assume, for example, that the rate of breakdown of photosensitive substance was proportional to the intensity of the stimulating light, the concentration of the photosensitive substance at any given moment, and the velocity constants of reaction in the retina. Thus he could write an equation for the "primary light reaction" as follows: $dx/dt = I(a - x)$, in which I is intensity of light; a is the original concentration of photosensitive material, x is the amount broken down at any time t. A similar equation was written for the "primary dark reaction": $dx/dt = x^n$, in which it is supposed that the photosensitive material is regenerated in proportion to the number n of photochemical byproducts and the amount x of photochemical deposed.

With these basic equations in hand, Hecht went on to combine the equations, integrate them, and elaborate them to explain various aspects of visual brightness—in fact, all the phenomena that we shall take up in this chapter. Once the equations were developed, they were fitted to the psychophysical measurements of vision made on human and animal subjects. In a surprising number of instances, the equations seemed to fit the data. Hecht and many others thought therefore that the fit was good evidence for the validity of the underlying assumptions.

Objections to the Theory. Certainly this approach has its merits. Indeed, there must be some large measure of truth in the photochemical theory and its mathematical formulations. There are, however, certain difficulties with it.

1. The theory assumed that all aspects of brightness vision could be explained in terms of photochemistry. It assumed a one-to-one relation between photochemical events in the retina and the brightness experience or discrimination of the organism which, we know, depends upon other events in the optic nerve and cortical and subcortical centers. In other words, Hecht put the burden of his theory on retinal photochemistry and left nothing for the nervous system or the brain to do.

2. There is always extreme danger in accepting a theory because the equations developed from it fit the data. These equations always contain two or

more constants whose values are not given by the theory but are adjusted as necessary to make the equation fit. In this case it is possible that many different equations, other than the one developed by the theory, will also fit the data. There is a common saying that an equation with two constants in it can be made to fit an elephant and one with three constants can make its tail wiggle. In a word, equations can be made to fit because their constants have been properly adjusted rather than because there is any fundamental merit in the equation.

3. More specifically, there are a number of instances in which the derived equations are contradicted by specific physiological data. You will see some of them in a moment. For these reasons, we cannot today accept the Hecht photochemical theory as more than a rough guide to our thinking about visual processes. We certainly cannot take it as the "correct theory."

Statistical Theory. An alternative to the photochemical theory has been the so-called *statistical theory* developed by Holway, Crozier, and their colleagues. This theory completely ignores photochemical processes, although it does not deny them. It assumes that the experience or discrimination of visual intensity is the over-all result of photochemical and neural processes and makes no attempt to identify the respective contributions of each. The fundamental premise of this theory is that the thresholds of the various elements of the visual system vary randomly in time—for which there is some evidence in neurophysiological work (Brink and Bronk, Lorente de No). From this assumption, a series of equations are developed to account for brightness vision. The basic form of all these equations is the probability integral, which is familiar to students of statistics.

One great merit of the theory is that it can fit quite satisfactorily a surprising number of the data of brightness vision (Crozier, Crozier and Holway). It suffers, however, like the photochemical theory, by having constants that can be arbitrarily adjusted to suit the needs of the theory. It also has the weakness of making an over-all mathematical formulation without identifying any of the individual processes in the chain of events from photochemistry to visual experience.

In the material that follows we are not going to elaborate or apply either of these theories. There are enough rather specific data to indicate that neither of these theories will be the ultimate form of our understanding of visual processes, and both theories take us too far afield into guesses, surmises, and mathematical bypaths. At some points, however, as we go along, we will show you how the facts bear on either of these theories.

LUMINOSITY FUNCTIONS

As we have already pointed out, brightness vision can be subdivided into absolute brightness sensitivity and differential sensitivity. Absolute sensitivity, with which we shall deal first, also depends upon a number of factors which can be examined separately: wave length, dark adaptation, light adaptation, and time. We shall take these up in turn.

The first of this list of factors affecting the absolute threshold of vision is wave length. And the relation between wave length and the threshold has a special name, the *luminosity curve. Visibility* curve or function is also a name applied to it. This is the threshold intensity of stimuli at various wave lengths of light. But there are not one but two luminosity functions. One, the *scotopic* curve, is what one gets when the eye has been in the dark for a long time and is at maximum sensitivity. The other, the *photopic* curve, is the curve one gets after the eye has been light-adapted to daylight levels of illumination. These two curves are another of the phenomena making part of the duplicity theory. You can see the two curves in Fig. 60. There you see that the scotopic curve has a peak at about 510 mμ, extending down to about 400 mμ and to a little above 600 mμ. The photopic curve has its peak about 550 mμ and extends to about 450 mμ and 700 mμ on either end. In Fig. 60 the two curves are arbitrarily drawn to the same height by adjusting each curve in terms of its point of maximum sensitivity. Actually, the eye is much more sensitive at scotopic levels than at photopic levels.

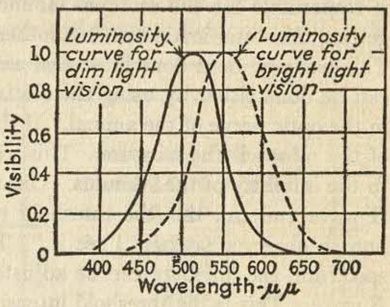


FIG. 60. The visibility (luminosity) curves for dim-light (scotopic) and bright-light (photopic) vision. Although sensitivity in bright light is poorer than in dim light, both curves have been adjusted so that their maxima are made equal to 1, and the sensitivity (1/I) at other wave lengths is expressed as fractions of the maximum. The maximum of the dim-light visibility curve is generally taken as 511 mμ and that of the bright-light visibility curve as 554 mμ. (*After Hecht and Williams. From L. W. Crafts et al. Recent experiments in psychology. New York: McGraw-Hill,* 1950. *P.* 131. *By permission of the publishers.*)

Luminosity and Spectral Absorption. Undoubtedly the first question that will occur to you is whether the scotopic luminosity curve is the same as the spectral absorption curve for visual purple. If that were the case, we would immediately have the physiological explanation of the luminosity curve. This curve would simply represent the degree to which different wave lengths of light are absorbed by the photosensitive visual purple of the rods. There is, indeed, such agreement in the final analysis, but there are two additional steps involved in the process (Hecht and Williams; Granit). One is to adjust the luminosity for quantum efficiency. Photochemical substances react in terms of number of quanta of light, and a light quantum varies with the wave length. By the appropriate calculations we can adjust our spectrum for equal number of quanta. Secondly, we know that the lens and optic media absorb light in the violet end of the spectrum before light gets to the visual purple. We know the factors for such absorption and can adjust the luminosity curve for them. The result of making these two adjustments is to find the luminosity curve and the spectral absorption of visual purple in very good agreement.

Neural Scotopic Functions. That the absorption spectrum of visual purple is responsible for the scotopic luminosity curve is further demonstrated by getting the scotopic function in another way by an electrophysiological method. This has now been done in several animals (Graham and Riggs; Granit). It can be done either by using the electroretinogram or by picking up impulses in the optic nerve of the animal. If the electroretinogram is used, the *B* wave of the record is the measure. This wave, you will remember, is proportional to the intensity of the stimulus. One can select arbitrarily a certain height of *B* wave and call this the threshold response comparable to the report of a human observer saying, "I see it." Then, with different wave lengths of the spectrum, the intensity can be adjusted until it just gives the right height of *B* wave. This is the threshold intensity. A scotopic luminosity curve of this sort corresponds with the curve obtained by visual methods from human observers. Moreover, when properly corrected for quantum efficiency and absorption of the optic media, it corresponds to the spectral absorption curve of visual purple.

It is also possible to record electrically the scotopic luminosity curve from individual retinal elements. By using a microelectrode technique, in which extremely small electrodes about the size of a nerve cell are employed, one can pick up impulses and use these as the threshold for response. Scotopic curves have been secured from the visual elements of the horseshoe crab (*Limulus*) in this way (Graham and Hartline) and from the ganglion cells of the retinae of several vertebrate animals (Granit). More will be said about the results of this technique in the next chapter, on color vision. There, too, we will consider the question of electrical measurement of the photopic curve, which, for reasons that you will see later, we will pass by now.

DARK ADAPTATION

Earlier, in talking about Hecht's photochemical theory of vision, we pointed out that there are two basic kinds of processes going on in the eye. One is light process, or light adaptation, in which the photosensitive material of the eye is broken down by light. If the sensitivity of the eye is dependent upon the amount of photochemical present—even in part—the eye should become less and less sensitive when stimulated by light. The second process is the primary dark process, in which the breakdown products of the photochemical plus additional sources of energy rebuild the photosensitive substance. Actually, this process will always go on whether or not the eye is in the dark. Thus both the light and dark processes will be occurring during light adaptation. When the eye is in the dark, however, only the dark process should be going on. That is why dark adaptation is a relatively simpler process than light adaptation and has been easier to measure experimentally.

Characteristics of Dark Adaptation. Figure 61 shows some of the major characteristics of dark adaptation. It shows, first of all, that the eye gradually increases its sensitivity in the dark. Second, it indicates that the speed of dark adaptation depends somewhat on the amount of previous light adaptation. If the eye has been exposed to a very intense stimulus, it regains its sensitivity in the dark much less quickly than if it has been adapted to a weak stimulus. Not shown in Fig. 61, but also true, is the fact that the longer the period of time for which the eye has been light-adapted, the slower the dark adaptation. A third characteristic is also shown in Fig. 61, that there are two more or less distinct segments in adaptation. There is one phase that levels out slowly, followed by a second phase in which dark adaptation speeds up and then finally slows down to its final low threshold. These two limbs of the dark-adaptation curve are more prominent in cases of high previous light adaptation than in cases of weak light adaptation but are nearly always detectable. These two limbs are one more evidence of duplicity of function in the eye. The first limb is ascribed to the cones, the second one to the rods.

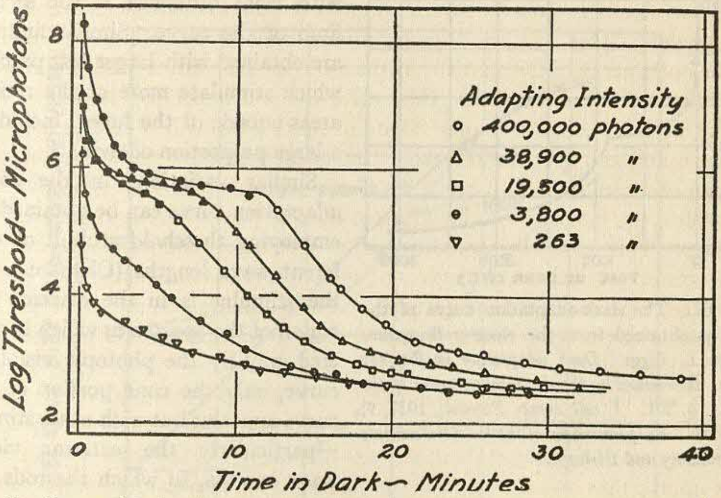


FIG. 61. Curves of dark adaptation following light exposures of different intensities. (*From S. Hecht et al. The influence of light adaptation on subsequent dark adaptation of the eye, p.* 837. *J. gen. Physiol.*, 1937, **20**, 831–850. *By permission of the Rockefeller Institute of Medical Research.*)

Duplicity Theory. The hypothesis that the two limbs of the dark-adaptation curve are related to cone and rod functions, respectively, is further confirmed by the relation of the dark-adaptation curve to the size and location of the photic stimuli used in securing thresholds during dark adaptation (see Chapanis). If the threshold stimulus is small enough and is put on the fovea, only the first segment of the curve appears, thus correlating this earlier part of the adaptation process with the functioning of the cones. On the other hand, if a small test spot is directed toward the periphery, which contains an overwhelming majority of rods, little if any of the first segment can be seen, but instead dark adaptation begins with what otherwise is the second limb of the curve. Similar findings are obtained with larger test patches which stimulate more of the retinal areas outside of the fovea, including a large proportion of rods.

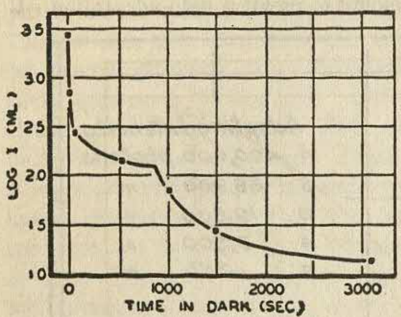


FIG. 62. The dark-adaptation curve of the frog as obtained from the electroretinogram. (*From L. Riggs. Dark adaptation in the frog eye as determined by the electrical reponse of the retina, p.* 501. *J. cell. comp. Physiol.*, 1937, 9, 491–510. *By permission of the Wistar Institute of Anatomy and Biology.*)

Similar variations in the dark-adaptation curve can be obtained by employing threshold stimuli of different wave lengths (Chapanis). If the stimulus is in the extreme red region of the spectrum, which is covered only by the photopic visibility curve, only the cone portion of the curve appears; but with other stimuli —particularly the extreme violet wave lengths, to which the rods are exclusively sensitive—the cone segment is less prominent and the rod segment much more so. Thus the duplicity theory is well supported by the facts of dark adaptation.

Retinal Basis. All that we have said so far points to the retina as the locus of the processes of dark adaptation. Should there be any question about that, however, we have definite experimental evidence in proof. By making use of the fact that the latency and height of the *B* wave of the retinal potential is a sign of the retinal effect produced by a stimulus, it has been possible to obtain dark-adaptation curves directly from the retina, thus ruling out the influence of the central nervous system (Riggs). The curve, shown in Fig. 62, was obtained from the eye of the frog, but it has just the same form as the curve given by human observers, including the two limbs representing cone and rod functions. There is left no doubt that retinal action is basic to adaptation and that it gives rise to the essential form of the adaptation curve. That is not to say, however, that the events expressed by the curve are not modified by central factors, for the whole visual system, both retinal and central, is necessary for the mediation of visual experience.

Dark Adaptation and Photochemistry. Having established that dark adaptation takes place in the retina, we can push the matter further by inquiring whether it can be understood in terms of regeneration of photosensitive material. We have no answer to this question for the cone substance, iodopsin. For visual purple, however, there is a good deal of information. It tells us that part, but perhaps not all, of the characteristics of dark adaptation of the rods are to be seen in the regeneration of visual purple (Hecht).

In Hecht's photochemical theory of vision, it is supposed that dark adaptation is the result of the recombination of two breakdown products of the decomposition of rhodopsin. Hecht called them *P* and *A*. If this notion is correct, the dark-adaptation curve ought to be fitted by a bimolecular equation (see Hecht, page 729). Certain of the data of human dark adaptation can, in fact, be fitted satisfactorily by this type of equation. When we take the data, however, for the actual regeneration of visual purple, we run into trouble. Several measurements of this regeneration have now been made, and one set of curves can be seen in Fig. 63 (Zewi). Attempts to fit these curves and others with the bimolecular equation have failed. The curves are all too straight at first and then taper off to a flat maximum too soon to fit the shape of the bimolecular equation (exponential). That is one strike against the straight photochemical theory of dark adaptation.

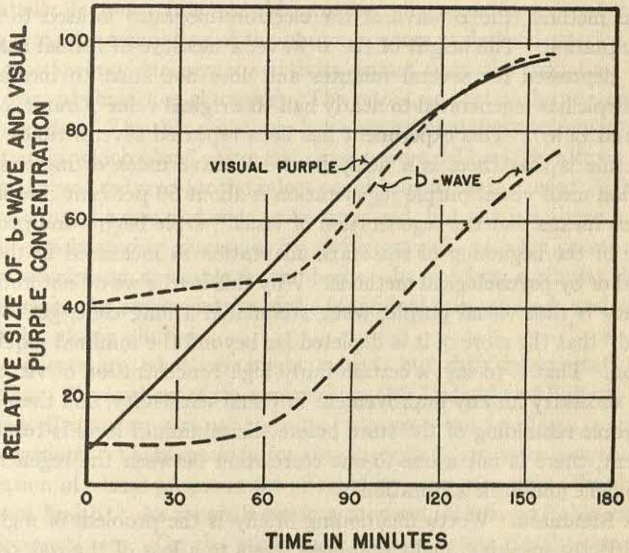


FIG. 63. Comparison of the regeneration of visual purple with dark adaptation measured from the *B* wave of the electroretinogram of the frog. The lower dotted line is for a weaker test stimulus than that used to get the upper dotted line. Note that the *B* wave does not begin to increase in size until visual purple has regenerated to about the 50 per cent point. (*After Granit, Munsterhjelm, and Zewi.*)

There is still another one to be seen by comparing the curves in Figs. 61, 62, and 63. You will notice in Figs. 61 and 62 that the rod curves of adaptation do not seem to begin until after several minutes in the dark. This is especially true of high levels of previous light adaptation. The rods seem to wait until the cones are through dark-adapting before they start their own adaptation. Yet when we look at what is happening to visual purple during this time (see Fig. 63), it is steadily regenerating. The delay in the adaptation of the rod portion of the curve is a real delay, too, for we can demonstrate it when a purely electrical method (the *B* wave of the electroretinogram) is used to measure dark adaptation. The height of the *B* wave, a measure of retinal sensitivity, remains depressed for several minutes and does not start to increase until visual purple has regenerated to nearly half its original value (Granit, Munsterhjelm, and Zewi). This experiment has been repeated several times, and the general rule is that there is a delay in the *B* wave index of increasing dark adaptation until visual purple regeneration is about 50 per cent complete.

All this means that the regeneration of visual purple begins and proceeds in advance of the beginning of real dark adaptation as measured in the retinal potential or by psychological methods. Why this is true we do not know. One possibility is that visual purple, when stimulated a long time, gets so "overbleached" that the store of it is depleted far beyond the minimal requirements for vision. That is to say, a certain fairly high concentration of visual purple may be necessary for any improvement in visual sensitivity, and there must be considerable rebuilding of the store before the minimum level is reached. In any event, there is not a one-to-one correlation between the regeneration of visual purple and dark adaptation.

Night Blindness. Worth mentioning briefly is the problem of night blindness. Strictly speaking, night blindness refers to a loss of the rod portion of the dark-adaptation curve, but in practice it sometimes includes deficiencies in the cone limb as well. One kind of night blindness, *hemeralopia*, appears to be a structural defect in the retina. In this type of defect, the rod portion of the curve never is seen at all and the cone portion remains completely intact. One would infer from this fact that there is a defect in the rods.

Another type of night blindness, of which we have heard much more in recent years, is ascribed to vitamin A deficiency. That there can be defects in dark adaptation—both of rods and cones—due to vitamin A deficiency cannot be questioned. In experiments in which people have suffered experimental vitamin A deficiency for many days, their threshold gradually rises. After 35 days of A-deficient diet, their final threshold may be as much as 2 log units higher (Hecht and Mandelbaum). Moreover, their entire dark-adaptation curves, both 'rod' and 'cone,' are raised. Whether vitamin A deficiency always produces night blindness and how it enters into the visual process are not clear.

Wald, one of the modern research workers in retinal photochemistry, has always considered vitamin A to be intimately concerned in the regeneration of visual purple—and probably also in that of iodopsin. In fact, he regards the visual white, the end product of photochemical decomposition, as made up in part of vitamin A. For this he has the evidence, presented by his own work and others, that vitamin A can be identified in the extracts of retinae that have been bleached by long and intense light before excision. Vitamin A always turns up in such extracts. Moreover, it has been well demonstrated that visual purple regenerates much more slowly in eyes suffering from vitamin A deficiency than in normal eyes (Tansley).

Metabolic Factors. It is probably worth saying something about the sources of energy for the rebuilding of the photoreceptors in dark adaptation. As you know, most energy for nervous activity comes from the oxidation of sugars (in the form of glucose or glycogen). The retina, as part of the nervous system, is no exception. On this point, we have experimental measurements of dark adaptation in which blood sugar and oxygen were deliberately altered. In one, blood sugar was reduced by the injection of insulin; this caused dark adaptation of both the cones and rods to be impaired, but the impairment could be offset by administering glucose or by giving oxygen—to burn up more rapidly the glucose already available in the body. In another, a similar decrement occurred when the oxygen intake of the individual was reduced, and this could be offset by giving glucose.

These effects are what one might expect, but their interpretation is also interesting. The authors of the experiments (McFarland and Forbes) supposed that these effects were due not to retinal processes but to effects in the central nervous system. Their grounds for this interpretation were reports that the regeneration of visual purple is not affected by oxygen supply (Wald; Oguchi; Chase and Smith). As we shall see in a moment, this is probably true under some circumstances. On the other hand, it now seems clearly demonstrated that in the final analysis, oxygen and presumably therefore glucose are necessary for the regeneration of visual purple.

In Fig. 64, you see the results of an experiment demonstrating this point (Zewi). The upper curve is one of regeneration of an intact eye with its normal blood supply. The middle curve is of an excised eye, deprived of its fresh stores of oxygen and glucose but still able to derive some oxygen from the air and some glucose from the tissues. The lower curve is of an excised eye kept in nitrogen without any access to oxygen. You see that without oxygen regeneration is impaired so that very little visual purple ever regenerates. It is probably safer, therefore, to interpret the effects of oxygen lack and glucose deficiency in terms of deficiencies in regeneration of photosensitive material rather than in terms of central nervous processes.

Two Modes of Regeneration. In order to bolster some of the points made above, it is probably well to point out that there are two modes of regeneration of visual purple (Granit, Wald). As we saw back in Fig. 55, one is a fast process which takes place from transient orange; the other is a slow one occurring from visual white, the final breakdown product of visual purple decomposition. The first fast process, we know, is not dependent upon temperature. It is probably also independent of oxygen or glucose or any immediate sources of energy (see above). The energy for this reconversion may come in part from the light itself, in part from accessory chemical materials in the cell which store energy for such immediate purposes. The slow process, on the other hand, must reach back into the reservoirs of material and energy in the blood and tissues adjacent to the photoreceptors. This regeneration we know to be affected by temperature, which is a sure sign that basic anabolic processes are going on. This regeneration, too, is dependent upon oxygen and glucose, as we pointed out above. And finally, it probably depends directly or indirectly on a source of vitamin A in the pigment cells adjacent to the photoreceptors.

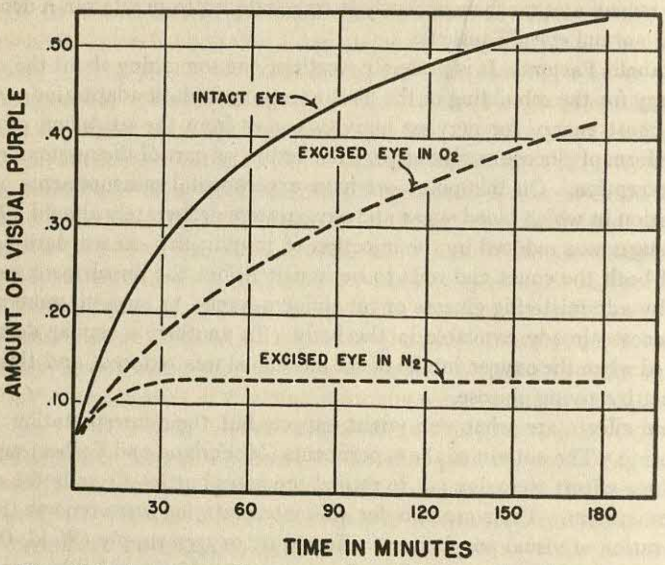


FIG. 64. The effect of oxygen on the regeneration of visual purple in frogs' eyes. Taking out the eye breaks off circulation of blood to the eye and slows regeneration somewhat. When the eye is both excised and deprived of all oxygen, however, there is some regeneration of visual purple, but very little and for only a brief period of time. The experiments were done at about 22°C., which is much colder than human body temperature, and the rate of regeneration therefore is much slower. (*Based on work of Zewi.*)

LIGHT ADAPTATION

By light adaptation we mean the change in sensitivity of the eye to continued stimulation by light. From what we have already covered, we would expect that continued exposure to light would break down photosensitive substances but also that this breakdown would be offset by the regeneration of visual purple. Thus any attempt to study photochemical events in light adaptation meets with not just one process but two going on simultaneously.

There is another difficulty we meet not only in making photochemical studies but also in making measurements of the changes in visual sensitivity of the human or animal subject during light adaptation. This difficulty is the rapid course of light adaptation, especially at its outset. Visual sensitivity changes so fast when the eye is exposed to light that it is changing while the observer is trying to make a judgment of what he can see.

The Light-adaptation Function. This particular difficulty has entered into almost all the measurements that have been made of human light adaptation. The values for the threshold have changed while the subject was making them. There is only one study that seems to have eliminated this and other minor objections that would make the result untrustworthy. In this study the subject was exposed to a field of uniform brightness, but every second after its onset an additional flash of light was superimposed on the center of the adapting field (Baker). The subject was asked to tell whether he could see this flash. The flash was adjusted in intensity very quickly to find the value that could just be seen by the subject. This situation is actually a brightness discrimination situation (which we shall study more carefully in the next section), but it is perfectly adequate for studying the course of light adaptation.

In Fig. 65 you see what Baker found. When the adapting light is turned on, the eye is relatively insensitive—the threshold is high. Immediately, however, the threshold plunges downward—the eye improves in sensitivity. Then, more slowly, the threshold gradually rises and settles on a plateau which represents considerably better sensitivity than at the start of light adaptation.

These are very interesting results, but they are not easy to understand in terms of photochemical theory. Such theory, and indeed what we know experimentally about photochemical materials, leads us to believe that the photosensitive materials are greater in concentration before light adaptation than after adaptation has been going on. Yet during this initial period the threshold of the eye gets better. The change is exactly contrary to what we would expect from simple photochemistry.

We might be tempted to doubt the data if it were not for other physiological facts confirming them. With electrical methods of measuring light adaptation in the optic nerve of *Limulus*, Riggs and Graham have obtained the same sort of results. They recorded nervous impulses while a light was turned on, and kept on, the eye of the animal. From their data they were able to compute the increment (ΔI) required to produce a certain number of impulses per second. The curve they came out with resembles that of Baker. At the beginning of light adaptation the threshold (ΔI) goes down, then later rises.

Although the facts seem clear, the explanation is not. Perhaps the only hint we have is one from recent work in photochemistry (Chase; also see Granit, page 225). This tells us that some sort of accessory substances or mechanisms are produced by the breakdown of visual purple and aid in its regeneration. These perhaps can make the eye more sensitive after a light is turned on than when it is in the dark. Some such mechanism, at any rate, is called for, but whether this is the one we do not know yet.

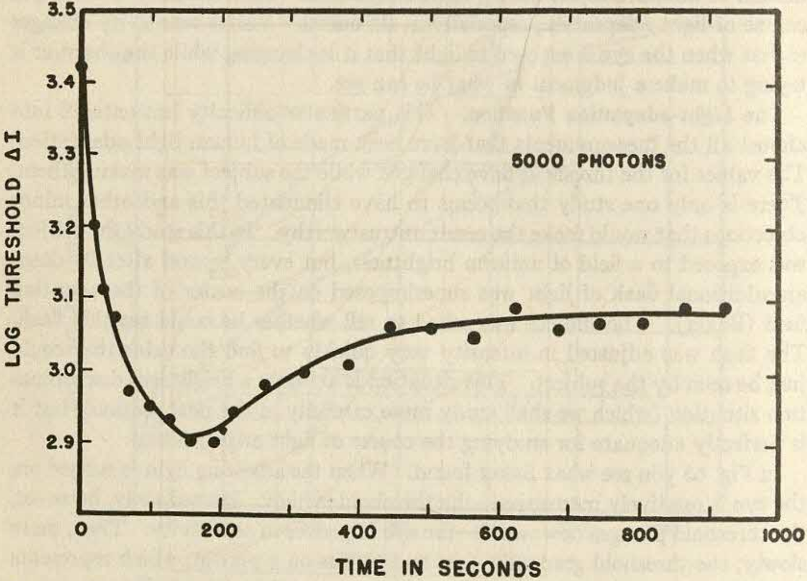


FIG. 65. The effects of light adaptation on the relative brightness threshold (ΔI). The base line is the length of time that an adapting light of 5,000-photon brightness is left on. The ΔI is the difference that can be detected between the adapting light and the test light. This is just a sample curve. Other curves for various intensities have been obtained. (*From H. D. Baker. The course of foveal light adaptation measured by the threshold intensity increment, p.* 176. *J. opt. Soc. Amer.*, 1949, 39, 172–179. *By permission of the American Institute of Physics.*)

BRIGHTNESS DISCRIMINATION

We may turn now to the topic of brightness discrimination. This is the detection of a difference in brightness between two slightly different intensities of light. It is customary to express brightness discrimination in terms of $\Delta I/I$, in which I stands for the standard intensity of light and ΔI is the increment of intensity that is just discriminable.

Brightness Discrimination. In Fig. 66 you see a characteristic set of curves for brightness discrimination. Here the logarithm of $\Delta I/I$ is plotted for different wave lengths of light at different intensities of illumination expressed in log photons (one of the units for measuring light intensities). The functions are arbitrarily displaced on the graph to avoid having them fall on top of one another. They show, as you might expect, two segments. The one to the left is the rod segment; the one on the right, the cone segment. The rod segment is missing from the upper curve, which represents a wave length of 670 mμ in the red, to which the rods and cones are equally sensitive. With all wave lengths, sensitivity in terms of $\Delta I/I$ is better at high intensities than at low ones. All these features of brightness discrimination are about what one would expect from our knowledge of visual functions.

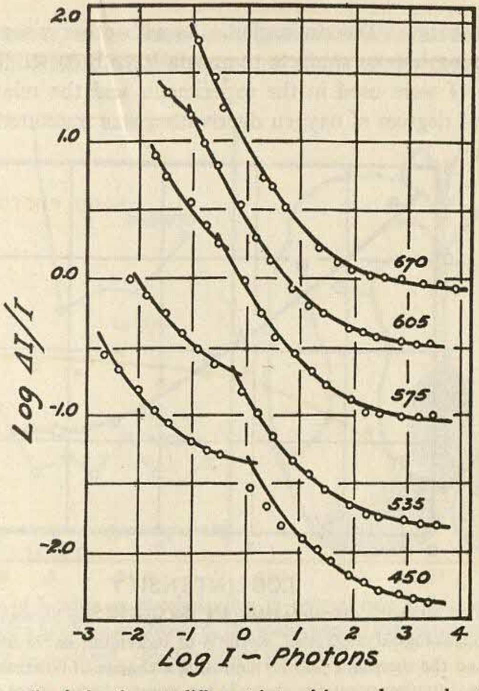


FIG. 66. Brightness discrimination at different intensities and wave lengths of light. The curve for 670 mμ (red) is displaced upward 1 log unit to avoid crowding on the graph; that for 605 mμ (orange), ½ log unit. The curve for 575 mμ (yellow) is not displaced at all. The curve for 535 mμ (green) is displaced downward ½ log unit, and that for 470 mμ (blue), 1 log unit. *(From S. Hecht et al. Intensity discrimination in the human eye: II. The relation between $\Delta I/I$ and intensity for different parts of the spectrum, p. 15. J. gen. Physiol., 1938, 22, 7–19. By permission of the Rockefeller Institute for Medical Research.)*

Retinal Processes. The electrical methods of measuring effects in the retina have not been put to work on the problem of brightness discrimination except in one case, the eye of *Limulus* (Riggs and Graham). In this case, the eye was adapted to a given intensity of illumination I, then exposed to an increment of illumination ΔI. The value of ΔI required to elicit a constant increase of the number of nerve impulses in the optic nerve was taken as the brightness threshold. The results are shown in Fig. 67. The invertebrate eye of *Limulus* contains only one type of receptor, not two, and it therefore gives a single unbroken function. In general, however, the function is similar to, although not so steep as, the psychological data for human brightness discrimination.

Anoxia and Brightness Discrimination. As with other visual functions, the effects of subjecting human subjects to anoxia have been studied. Three different values for *I* were used in the experiment, and the relative increase in $\Delta I/I$ for different degrees of oxygen deprivation was measured. One can see that even mild amounts of anoxia produce measurable impairment of brightness discrimination. The interpretation of this fact, however, is a debatable matter. The investigators who did the experiment (Hecht *et al.*) feel that the impairment occurs in the central nervous system, not in the retina. Yet until we are more certain about the role that oxygen plays in the regeneration of photosensitive substances of the retina, it might be well not to jump to conclusions. In fact, if some physiologists (Granit) are correct, these changes may well be due to photochemical processes in the retina.

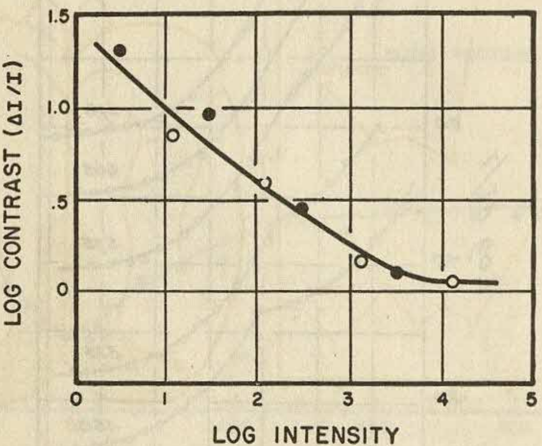
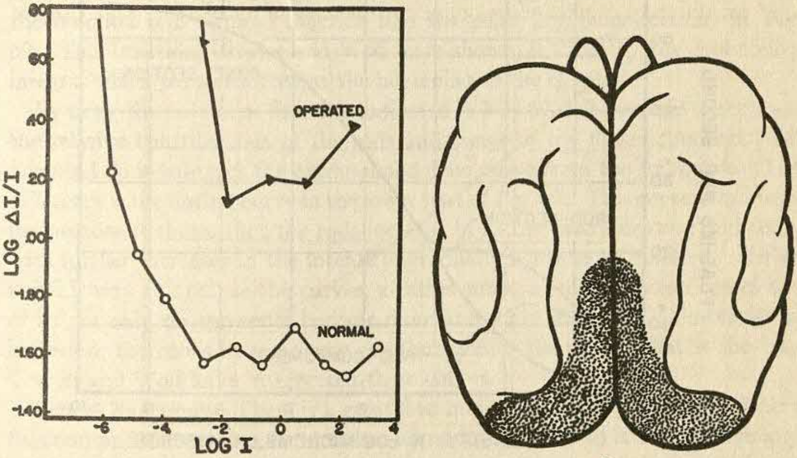


FIG. 67. A curve of intensity discrimination for the eye of the horseshoe crab (*Limulus*) gotten by electrophysiological methods. Records of individual nerve impulses in receptor cells were taken, and the threshold (ΔI) for detecting a change in illumination (I) was taken as an increase of two impulses occurring about ⅔ sec. apart. (*After Riggs and Graham*, 1945.)

The Cerebral Cortex and Brightness Discrimination. There are now a good many experiments telling us about the role of the central visual system in brightness discrimination. All the mammalian animals except possibly man seem able to discriminate brightness after the removal of the visual cortex. If, as we shall see later (page 470), certain kinds of training methods are used to build up the discrimination in an animal, it may lose the habit when its cortex is taken out. This phenomenon, however, is one of memory rather than capacity, for the animals can discriminate brightness again after retraining (Lashley, Smith). We may conclude, then, that the visual cortex is not solely responsible for the capacity of brightness discrimination, as it is for spatial vision.

There are, however, some losses in brightness discrimination after cortical 'blinding.' When careful measurements are made of the thresholds ($\Delta I/I$ of brightness discrimination), there is a sizable impairment in brightness discrimination. Mead's experiments with cats, illustrated in Fig. 68, demonstrate this fact quite clearly (see also Bridgman and Smith). The whole curve is shifted upward about a logarithmic unit, that is to say, by a factor of 10. Apparently, then, the visual cortex has something to do with good brightness discrimination but shares this function with the subcortical visual center, presumably the superior colliculus.



A *B*

FIG. 68. *A*, curves of brightness discrimination in normal cats and in cats in which the visual area of the cortex has been removed; *B*, the visual area of the cortex of the cat. (*From unpublished results by L. C. Mead. By permission of the author.*)

A word of caution is in order about the interpretation of this impairment. We have already seen that the visual cortex is necessary for spatial vision. The cats in these experiments were run in boxes in which they had to find their way to the correct door in order to make the discrimination. It is possible that the apparent impairment in brightness discrimination is due to the deficit in space perception needed to solve the discrimination. We will be sure only when we have other results based on a technique not handicapped with this difficulty.

FLICKER DISCRIMINATION

Last of the aspects of brightness vision to consider is flicker discrimination. This is the detection of changes in brightness in a light that is going on and off at a rapid rate. The threshold for such a discrimination is called the *critical flicker frequency* and is usually abbreviated as *c.f.f.* The c.f.f. is the lowest frequency of the flashing of a light that is perceived as steady or conversely the highest frequency perceived as intermittent. Flicker discrimination rightly belongs with the discussion of brightness vision, for it is basically a matter of discriminating alternations in the brightness of stimuli.

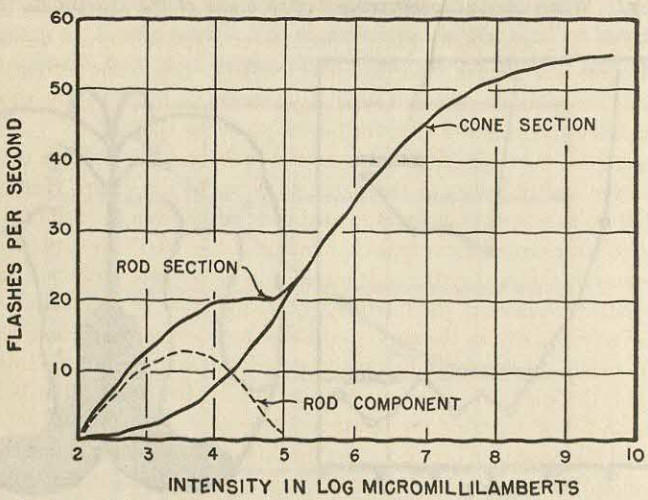


FIG. 69. Analysis of the curve for flicker discrimination as it has been made by Crozier and Wolf. The lower solid curve is for the all-cone area of the fovea. The other solid line is for parts of the retina that contain both rods and cones. The dotted line is the difference between the rod and cone curves. It seems to indicate that rods are active in flicker discrimination only at low intensities and are inhibited at the higher intensities. Functions in this graph are only approximate and are altered somewhat by various conditions of measurement. (*After Crozier and Wolf,* 1941.)

The Flicker Function. Perhaps no other visual function has been so often and so accurately measured as the relation of flicker discrimination to visual intensity. Many of the lower animals give reflex movements of the head, eyes, or body to flickering stimuli, and these movements can be used for measuring c.f.f. under many different circumstances in many different animals. In Fig. 69 appears a typical flicker function for the human observer. It indicates that the c.f.f. varies from 2 to 3 cycles per second at very low intensities to about 60 cycles per second at high intensities. The curve also shows a clear division into a rod segment, at low intensities, and a cone segment at high intensities. This is the typical curve that is found in all eyes possessing both rods and cones.

As we shall see in the next chapter, however, there are some animals with only rods in their eyes and others with only cones. The flicker functions measured in such animals are of some interest because they tell us exactly how to break down the duplex function seen in Fig. 69. As you might expect, flicker functions in pure-cone or pure-rod eyes are simple continuous functions not broken into segments. Even more interesting, however, is the fact that the function is a sigmoid function like the solid line (cone-section) in Fig. 69. This function, Crozier and Wolf have shown, is fitted by the probability integral which we considered at the beginning of the chapter.

By using the pure-cone function indicated in Fig. 69, it is possible to separate the relative contributions of the rods and cones to the flicker function. All one need do is subtract the extrapolated cone curve from the rod curve. The difference is the dotted curve in the lower part of Fig. 69. This curve is interesting because it shows that the rods increase in flicker discrimination and then, with further increases in the intensity, gradually come to be inactive. If this is a fair way to analyze the curves, a rather unexpected conclusion comes out of it: not only do the cones become more and more important as intensity is increased, the cones in some way or other inhibit the rods. That is the way Crozier and Wolf have interpreted these curves.

Retinal Functions. There is a great deal more we could say about the flicker function and the various factors that affect it, but little of it would have any bearing on the physiological processes in vision. Such processes, which are our main interest here, have been attacked in only a few experiments. The retinal potential, for example, has been recorded in different animals while stimulating the retina with a flickering light (Granit and Therman). One thing that is clear in these studies is that the retinal potential does not accurately reflect the perception of flicker (see Granit). The record of the retinal potential will show alternations in it corresponding to the rate of the flickering light. As the rate of flicker is increased, however, the retinal record becomes fused long before the flicker fusion threshold. The maximum rate of flicker for fusion in the retinal record, for example, varies between 20 and 40 cycles per second for different eyes, although the c.f.f. goes up to 60 cycles or even higher. That fact, however, should not disturb us, because the retinal potential is a sort of average of activity in the retina and does not reflect the behavior of individual units in it.

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CHAPTER IX

COLOR VISION

If we were using catchy titles for our chapters in this book, this one would be "The Mystery of Color Vision," for that is what it is—a mystery. We do not at the present time have a satisfactory understanding of the physiological processes that underlie color perception. We have been making progress, however, for the last few years have brought forth many new data as well as suggestions for the solution of the mystery. We shall present them to you here.

THE STRUCTURE OF THE RETINA

You have already gotten acquainted with the general features of the retina. There are, however, some aspects of the interconnections of retinal elements which we have not emphasized and which are especially relevant to the problem of color vision. There are, moreover, some questions about the nature and function of the rods and cones which up to now we could avoid because they were not important. Now, however, we ought to face them squarely in considering possible physiological mechanisms of color perception. Let us start with the topic of rod and cone receptors.

Rods and Cones. It is easy and convenient to talk about rods and cones as though they were two distinct types of elements. When we stop and examine some of the facts about them, however, we have cause for concern about carrying the distinction too far.

For one thing the different structures of rods and cones cannot always be clearly distinguished. To get some appreciation of how cones and rods vary in structure in different animals and in the human retina, study carefully the drawings in Fig. 70 (Willmer). These are drawings of the photoreceptors of four different vertebrate animals. In *A*, you see those of the frog, which divide themselves fairly well into cones and rods. They look like their names, the cones being short and pointed and the rods being long and cylindrical. In *B*, you see the rods and cones of the house sparrow. Again they seem to be fairly well distinguished, but the cones look a little more like rods, and one kind of rod (3) comes fairly close to looking like a cone. In *C*, the receptors of man, the situation becomes even more disturbing. To be sure, there are many cones from the various regions of the peripheral retina (6) that look like cones, and the rod looks like a rod. But look at what is supposed to be the cone found in the *fovea centralis*—the all-cone area of the fovea (7). This 'cone' outdoes the rods in being long, cylindrical, and rodlike. The only excuse for calling this element a cone is that it is situated in the fovea, where all the elements are supposed to be cones because they discriminate color and do not show any 'rod'

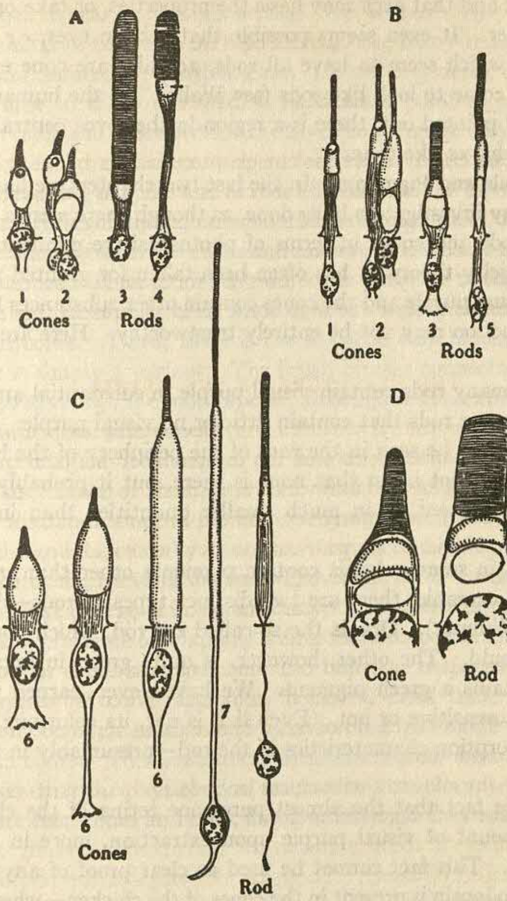

FIG. 70. Drawings of "rods" and "cones" found in the eyes of different vertebrates. *A*, the leopard frog; *B*, the house sparrow; *C*, man; and *D*, the mud puppy. 1, typical cone; 2, so-called twin cone; 3, typical red rod; 4, green rod; 5, rod from the central area; 6, cones from different regions of the periphery of the retina; and 7, cone from the fovea. For further explanation see text. (*Based on work of Arey and Walls. From E. N. Willmer. Retinal structure and colour vision. New York: Cambridge, 1946. P. 2. By permission of the publishers.*)

part of the dark-adaptation curve (Fig. 61). Another comparison of rod and cone is given in *D* of Fig. 70 for the mud puppy (an amphibian). Here the so-called rods look very much like cones, although they can still be distinguished.

These are just examples of what one encounters in the retinae of various vertebrates. Histologists (Walls, Willmer) who have studied these retinae carefully conclude that the differentiation between rods and cones is by no means clear-cut and that each may have the properties, or take on the properties, of the other. It even seems possible that certain eyes, *e.g.*, that of the lizard (gecko), which seem to have all rods, actually are cone eyes in which the cones have come to look like rods (see Walls). In the human retina, too, as we have just pointed out, there is a region in the fovea centralis that looks like rods but behaves like cones.

Photochemicals and Pigments. In the last two chapters we have been talking, just as many investigators have done, as though there were a clear separation between rods and cones in terms of photosensitive pigments of the eye. Under the duplicity theory, it has often been taken for granted that only the rods contain visual purple and the cones contain other substances like iodopsin. Even this distinction may not be entirely trustworthy. Here are a few of the reasons.

1. Although many rods contain visual purple in substantial amounts, there are apparently some rods that contain little or no visual purple. At any rate, no visual purple can be seen in the rods of the periphery of the human retina (Arey). This may not mean that none is there, but it probably means that visual purple, if present, is in much smaller quantities than in the typical rod.

2. Some rods in some animals contain pigments other than visual purple. In the frog, for example, there are two distinct types of rods—distinct as to color (Kühne, Willmer). One is the so-called *red* rod, which contains visual purple as it should. The other, however, is quite green in appearance and apparently contains a green pigment. We have never learned whether this pigment is photosensitive or not. Even if it is not, its color ought to change the spectral absorption characteristics of the rod—presumably in the direction of the red.

3. Finally, the fact that the almost pure-cone retina of the chick yields a considerable amount of visual purple upon extraction, more in fact than of iodopsin (Bliss). This fact cannot be used as clear proof of anything, but it suggests that rhodopsin is present in the cones of the chicken—where, according to the duplicity theory, it should not be.

Retinal Synapses. Whatever may be the different functions of rods and cones or of different types of rods and cones, their activity is certainly altered in the course of relaying messages through the synapses of the retina. There may, of course, be a good deal of order in the synaptic connections of neurons that cannot be seen by the eye of the histologist. It is nevertheless difficult to see how the impulses reaching the ganglion cells through the bipolar cells of the retina could escape the many possibilities of interaction and modification in these synapses.

Modern histology gives us a very detailed description of the retinal cells and their connections (Polyak, Walls, Willmer). There are, as you already know, certain cells that make lateral connections between rods and cones and between various bipolar and ganglion cells. We have already pointed out, too, that the rods tend to converge on bipolar cells, *i.e.*, many rods connect with a few bipolar and, indirectly, ganglion cells. Cones, in general, do not converge so much. Those in the fovea tend to maintain a point-to-point connection with ganglion cells, and those outside the fovea converge to only a small degree.

Aside from these lateral and convergent features of the retina, there are other sources of overlapping of cones and of rods and cones in the bipolar connections. Three main categories of bipolar cells have been distinguished. One, the midget bipolar, connects only with the cones and maintains the point-to-point connection just mentioned. It maintains a 'pure' cone pathway to the ganglion cells. Second, there are flat bipolar cells, some of which supply cones only and some both rods and cones. Third, there is the so-called *mop* bipolar, of which the brush bipolar is simply a variant. The brush bipolar connects with both rods and cones. So also does the mop bipolar, although it generally connects more with rods than it does with cones.

As you may imagine, it is easy to get into all sorts of details in discussing the connections. Most of them, however, would be of little help. The only central point that stands out in the maps of synaptic connections in the retina is that the cones and rods usually do not have separate pathways to the ganglion cells and hence to the nervous system. The exception is the small area of the fovea centralis that is so good in visual acuity. This area has 'straight through' paths without appreciable overlapping. And there may be a few such 'straight through' paths for cones scattered here and there in the periphery of the eye. The vast majority of cones and rods, however, must 'talk to' the central nervous system through bipolar and ganglion-cell pathways being used by other rods and cones. This anatomical situation means—and this point must be emphasized—that the physiological mechanisms of color must involve many interactions between cones and rods, however different they may be as specific receptors.

THE MICROPHYSIOLOGY OF COLOR RECEPTION

With this discussion of the retina in mind, let us move on to another new and exciting phase of the research on color vision. This is the recording of activity in individual pathways of the visual system. More particularly, it is the study of responses of individual fibers of the ganglion cells of the retina with lights of different wave length. We may think of it as the microphysiology of color reception.

Microelectrode Technique. To get specific knowledge of what individual receptors and neurons may do when the retina is stimulated with 'colored' lights, a Swedish physiologist named Granit has developed a method frequently called the *microelectrode technique*. Hollow glass tubes are drawn out by means of a special heating and stretching apparatus until their tips are only a few microns in diameter—approximately the same size as the individual neurons of the retina and nervous system. These extremely small glass filaments are filled with fine silver wire or physiological saline solution to make a conducting electrode. This electrode is mounted in a special holder that can be moved extremely small distances by knobs and gears much like those of a microscope stage. In this instrument, called a micromanipulator, a freshly excised eye can be mounted for study.

Surgical Approach. There are several points of technique in this kind of work that ought to be brought out so that you will understand the nature of the results obtained. In the first place, the microelectrode is applied to the retina by removing the lens and cornea of the eye and lowering the electrode down through the inside of the eyeball. As you will remember from an earlier section (page 157), the lens and the cornea absorb light in the violet region of the spectrum. Thus when they are removed, the retina gets more of any such light used to stimulate it. The curves one gets, whether they be luminosity curves or the component curves which we shall describe in a minute, will always show higher absorption in the blue end of the spectrum than we could expect in the intact eye. On the other hand, the results one gets without the lens and the cornea can be directly compared with the absorption spectrum of visual purple (see page 148). These reflect the true characteristics of retinal absorption uncontaminated with the absorption properties of the optic media.

Recording from Ganglion Cells. Second, when the electrodes are lowered to the retina from within the eyeball, the first point of contact is with the fibers of the ganglion cells of the retina. You will remember that in the vertebrate eye the retina is inverted in such a way that the ganglion cells and their fibers face the pupil of the eye and the source of stimulating light. It is to be presumed, therefore, that all the results coming from the microelectrode technique represent activity in the ganglion cells and not in the primary photoreceptors or bipolar cells. That is an important point, for it means that the microelectrode technique records the kinds of 'messages' that are going into the brain after the rods, cones, and bipolar cells have interacted with one another.

Recording from Individual Units. Third, it is usually possible for the microelectrode to pick up activity in a *single* ganglion-cell unit. Of course, the microelectrode, small as it is, is larger than the particular unit. On the other hand, by micromanipulation of the electrode it is possible to get the electrode nearer to one unit than to another and to pick up responses that can be ascribed to one unit. To do this, the electrical activity is amplified and presented on an oscilloscope. The responses which are strongest and which the electrode picks up best are the biggest responses seen on the oscilloscope. Fortunately, because of the all-or-none law of nervous impulses, it is possible to sort these big responses out from the smaller ones. The larger responses will always appear at the same height; smaller responses will also be of constant height, but lower. This fact, together with slight manipulation of the place of the electrode, allows the experimenter to pick out the responses of single units from the spikes that appear on his oscillograph.

Measurement of Thresholds. Finally, it is possible to determine the spectral sensitivity of the units being studied by changing the intensity and wave length of light with which the retina is stimulated. When an experimenter has found a unit on his oscilloscope that can be identified and separated from any other units, he can reduce the intensity of light on the retina until a threshold for the unit can be found. Such a threshold can be established arbitrarily as the intensity necessary to evoke one impulse, two impulses, or any other number of impulses in a given period of time after the light has been turned on. Whatever the criterion of the threshold, it must be followed consistently in one experiment. Then the wave length of the light can be varied through the visible spectrum to see how the threshold of the unit depends upon the wave length of the light.

These are the important points about the microelectrode technique. Now we shall go on to some of the results. At the present time, several different animals representative of the vertebrate series have been investigated. Some have pure-rod eyes, some pure-cone eyes and some are of the mixed type, similar to the human retina. It will serve best to bring out the important points if we consider these three kinds of retina in turn.

THE PURE-ROD RETINA

There are a good many animals in the vertebrate series that appear to possess only rods in their eyes. Two of these studied by the microelectrode technique are the rat and the guinea pig. Everyone who has studied the histology of the guinea pig retina seems to agree that it has an all-rod eye. On the rat, however, there is not complete agreement. Certainly the overwhelming percentage of the receptors in the rat's eye are rods, but there are a few receptors here and there that look something like cones. Some histologists (Walls) think they are cones, but others (Detwiler) do not. At any rate, the microphysiological results are interesting and instructive.

Responses of the Rat Retina. If the rat has a pure-rod retina, you would expect it not to show any evidence of special color mechanisms and to display only the typical scotopic luminosity curve that is characteristic of rod vision. That is what would be predicted by the classic duplicity theory, but that is not what happens. In Fig. 71 you see the typical response of optic fiber of the rat's retina. It has two 'humps,' one at 500 mμ and one at 600 mμ. The hump at 500 mμ you will recognize immediately as the typical curve for visual purple and the scotopic visibility curve of the rods. Actually, there are some minor differences between the microelectrode curve at 500 mμ and the absorption spectrum of visual purple, but we do not need to go into that problem here (see Granit). The hump at 600 mμ, however, seems to indicate the presence of a color receptor. Here are some of the reasons why.

1. The two humps react differently to light and dark adaptation. In Fig. 71, you see that the 600-mμ hump is very resistant to light adaptation and does not change much in sensitivity during dark adaptation. It behaves in about the same way as the cone limb of the human dark-adaptation curve. The hump at 500 mμ, however, changes considerably in sensitivity during dark adaptation. After an initial delay of several minutes, the threshold at 500 mμ decreases markedly. In fact, this hump behaves in dark adaptation somewhat like the rod portion of the human dark-adaptation curve. This behavior of the two humps, therefore, gives the appearance of there being two receptors, not one, involved in the record.

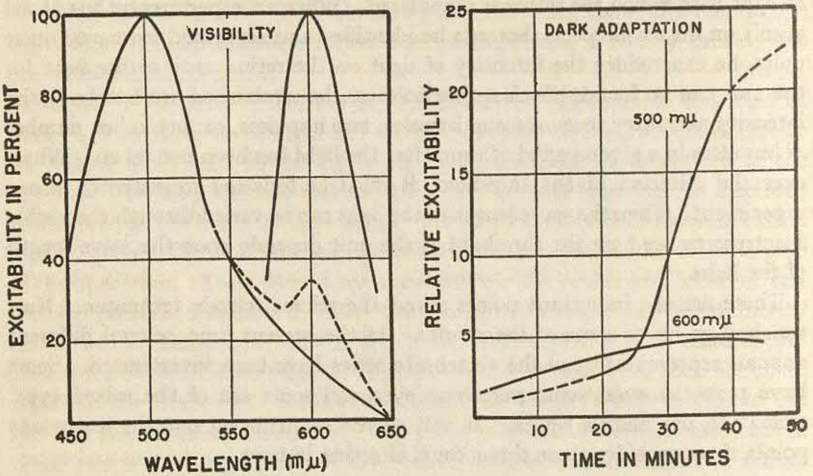

FIG. 71. Responses of cells in the retina of the rat. The peak at 500 mμ is a 'scotopic' receptor—probably a rod. It bleaches easily in light but regains its sensitivity in the dark (see curve on the right). The peak at 600 mμ, sometimes coupled with the rod curve, seems to be a 'red' receptor. It becomes prominent when the rod curve is bleached by light. Its sensitivity changes very little with either dark or light adaptation. (*After Granit.*)

2. It seems rather clear that these two receptors are so joined together by bipolar cells, or by something, that they discharge their effects to common optic fibers of ganglion cells. All the records that Granit has from the rat's retina show that the two humps are always coupled together, *i.e.*, by appropriately dark-adapting or light-adapting the eye, both humps can be made to appear while the microelectrode remains in contact with the same optic fiber. This demonstrates physiologically the coupling of several rods and cones which we described in the synaptic structure of the retina above (page 175).

Finally, we come to the question of what kinds of receptors these two humps at 500 and 600 mμ represent. This hump at 600 mμ is something we shall meet in practically every eye we shall consider. Moreover, it is the 'longest' hump that is ever found, *i.e.*, no humps of longer wave lengths than 600 mμ ever turn up in microelectrode work. It therefore must be the 'red' receptor of the vertebrate eye. To be sure, 600 mμ, when presented to the human eye, does not look red but, rather, orange. That is probably due, as we shall see later, to stimulation by this wave length not only of the 'red' receptor but of other receptors too. It is nevertheless proper that we speak of the 600-mμ receptor as the 'red' receptor.

In the case of the rat, therefore, we may say that it possesses a 'red' receptor. If the rat has any cones, this 'red' receptor might be a cone, but we do not know. Moreover, to say that the rat has a 'red' receptor is not to say that it sees 'red,' for the rat might not have the central nervous equipment to make use of such a receptor. It happens, however, that there is now rather acceptable evidence that the rat can, in fact, discriminate red (Walton).

The Scotopic Curve of the Guinea Pig. The guinea pig, as we have already indicated, has an eye regarded as a pure-rod eye. In doing microphysiological studies of this eye, several different curves with their humps in different regions have been identified (Granit). One of them, with a hump at 500 mμ, can certainly be identified with visual purple and the scotopic luminosity curve. In Fig. 72, you see that the sensitivity of the element coincides with that of visual purple and, after correction for the blue absorption of the lens and optic media, with the scotopic luminosity curve of the dark-adapted eye. These elements have been found in the guinea pig eye uncontaminated by humps in other regions. We can therefore feel sure that there are some rods in the guinea pig retina not coupled to color receptors, which behave as rods should according to the duplicity theory.

'Narrow' Curves of the Guinea Pig. The surprising thing, however, about the all-rod retina of the guinea pig is that it gives evidence of having several color receptors. By micromanipulation of the electrode in its retina, optic fibers can be found that show the scotopic curve coupled with humps in other regions. Indeed, some fibers can be picked up that show curves completely different from that of the scotopic luminosity curve. These other curves have been called modulator curves by Granit, but we prefer to call them simply *narrow curves* to distinguish them from the broader scotopic and photopic luminosity curves.

Altogether, three different narrow curves have been found in the guinea pig retina: one at 460 mμ, in the blue region of the spectrum, one at about 530 mμ in the green region, and one at 600 mμ, which we have already called the 'red' component or receptor. The 'red' component at 600 mμ is very rare in the guinea pig but probably exists. In one experiment in which it turned up, it was coupled with the scotopic curve (peak at 500 mμ) in much the same way that it appeared in the rat. A narrow 'green' curve with its peak at 520 or 530 mμ, however, is sometimes seen all by itself. We can be quite certain therefore that a 'green' receptor exists in the guinea pig which is sometimes uncoupled with any other type of receptor. Finally, a 'blue' hump at 460 mμ very frequently appears in conjunction with the 'green' curve. When it does it may sometimes be higher, sometimes lower, than the 'green' hump. We can therefore conclude that a 'blue' receptor exists and that usually, if not always, it is coupled with the 'green' receptor.

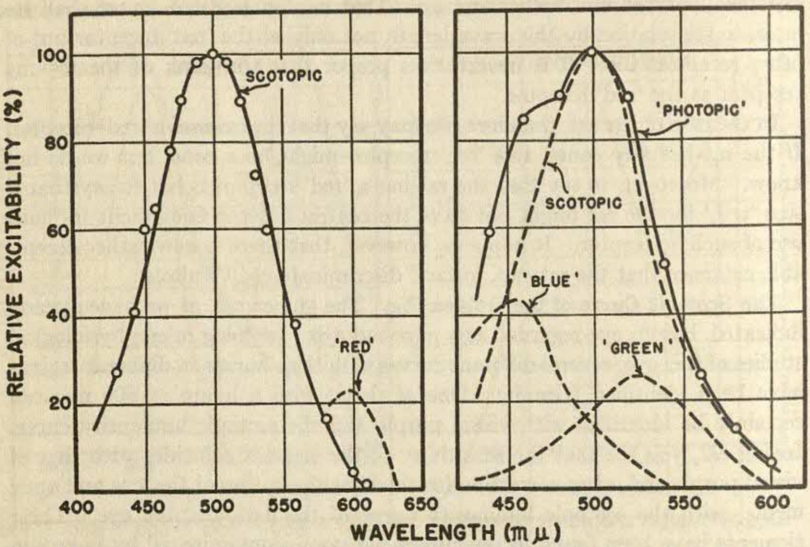

FIG. 72. Curves of spectral sensitivity from cells in the retina of the guinea pig. In addition to the typical scotopic 'rod' curve seen on the left, several other curves representing different color receptors appear. The 'red' receptor is often coupled with the 'rod' curve. Peaks in the 'blue' and 'green' also are obtained. These various peaks seem to combine to make the 'photopic' curve that can be gotten in the records. (*After Granit.*)

The picture, then, for the guinea pig retina is that it contains the scotopic rod receptor with the absorption spectrum of visual purple and three 'color' receptors, a 'blue' one, a 'green' one, and a 'red' one. The 'green' one is common and can show up alone in the response of optic fibers. The 'blue' receptor is usually coupled with the 'green' one. The 'red' one is rare and when seen is coupled to the scotopic receptor. Perhaps the most important conclusion from these facts is that the receptor equipment for color vision can be present in a pure-rod eye—a strong blow for the duplicity theory. Whether or not the guinea pig can see and make use of color, however, we do not know, for the appropriate psychological experiments have never been carried out.

Pure-cone Retina

It is fortunate that nature provides us with different types of eyes, some pure rod, some pure cone, and some mixed, for otherwise we would have a difficult time separating out responses of the rods and cones. Thus, in addition to the pure-rod eyes of the rodents, there are some pure-cone eyes which can be studied. For some reason these are found most abundantly in the reptiles. One type of snake[1] with a pure-cone retina has been selected for study by microelectrode methods (Granit). Here is what it tells us.

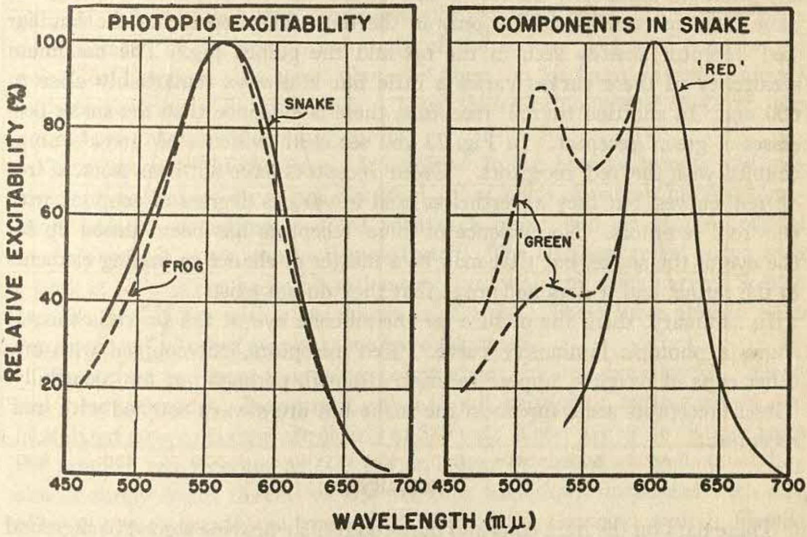

Fig. 73. Curves of spectral sensitivity of cells in the retina of the snake and the frog. The snake has a pure-cone retina. It has peaks of sensitivity in the 'green' and the 'red,' sometimes coupled and sometimes not. Photopic curves can be gotten in both the snake and the frog (mixed rod and cone retina) that resemble the photopic curve in man. (*After Granit.*)

Photopic Sensitivity. Just as the duplicity theory would predict, the snake has a photopic luminosity curve. In rats and guinea pigs, with pure-rod retina, the microelectrode never picks up any fibers with the photopic (light-adapted) sensitivity curve seen in man. On the other hand, in the pure-cone retina of the snake, the scotopic (dark-adapted) luminosity curve typical of rod vision in man and other animals is never found. Some of the optic fibers that have been studied, however, give a photopic sensitivity curve with a peak at 560 mμ, just as one would predict for the cones. In Fig. 73 you see such a curve for the snake (Granit). We shall see later that mixed eyes also give such photopic curves.

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[1] The all-cone retina of a tortoise has also been studied and shows the same general picture as the snake. For some reason, however, the photopic luminosity curve of the tortoise is more like that of the 'visual violet' fishes (those containing visual violet rather than visual purple) than like that of the higher vertebrates (see Wald). For the details of this problem, see Granit, pages 200 and 293.

'Red' and 'Green' Curves. By hunting around in the retina of the snake, it is possible to find fibers that have curves of sensitivity quite different from the photopic luminosity curve. A few of the curves, as you see in Fig. 73, have their spectral sensitivity only in the red. This represents the familiar 'red' receptor already seen in the rat and the guinea pig. The maximum sensitivity of these curves varies a little but is always remarkably close to 600 mμ. In addition to 'red' receptors, there is evidence that the snake possesses a 'green' receptor. In Fig. 73 you see clear evidence of 'green' humps coupled with the 'red' receptors. 'Green' receptors have not been isolated free of 'red' curves, but they nevertheless exist in various degrees of coupling with the 'red' receptors. No evidence of 'blue' receptors has been turned up for the eye of the snake, but that may be a matter of chance in finding elements in the retina, and it does not prove that they do not exist.

In summary, then, the picture for the all-cone eye of the snake is this: It shows a photopic luminosity curve. 'Red' receptors, not coupled with any other type of receptor, appear to exist, although perhaps not too plentifully. 'Green' receptors are common in the snake but are always coupled with 'red' receptors.

MIXED EYES

These data on the pure-cone and pure-rod retinae provide a good background for the discussion of eyes of mixed types—those containing both rods and cones (Granit). We shall see that the 'blue' receptor at 460 mμ, a green receptor at 530 mμ, and a red receptor at 600 mμ are also found in the mixed eyes. In addition we shall see evidence for a 'yellow' receptor with maximum sensitivity at 580 mμ.

The Purkinje Shift. First, however, it is interesting to note the behavior of scotopic and photopic luminosity curves in the mixed retinae. In all mixed retinae—fish, frog, pigeon, and cat—there is a Purkinje shift. That is to say, the scotopic luminosity curve can be obtained from optic fibers when the eye is dark-adapted, and the photopic luminosity curve can be measured when the eye is light-adapted. In fish which possess visual violet, rather than visual purple (Wald), these curves are displaced toward the long wave lengths, but they can nevertheless be recorded and they correspond with the known scotopic and photopic visibility curves of the animal measured by behavioral methods. The microphysiological methods thus confirm nicely the psychophysical data.

There is a very important point about the Purkinje shift shown with the microelectrode technique. *The shift occurs in the record of a single optic fiber.*

A particular fiber can be found with a microelectrode in the dark-adapted eye that will give the scotopic luminosity curve. This same fiber, however, will give the photopic curve after the eye has been light-adapted. This fact means one of two things—we cannot tell which: either the Purkinje shift occurs within a single receptor and does not represent a shift from a rod to a cone receptor, or the two different receptors involved in the shift are coupled to the same bipolar cell or ganglion cell or both. The latter possibility, perhaps, is the more probable, in view of the fact that the microelectrode probably records from the ganglion-cell fiber and that convergence of rods and cones has already been demonstrated in the anatomical study of the retina. We should hasten to point out, however, that some 'photopic' fibers can be found in some animals without showing a Purkinje shift. Thus photopic luminosity functions are not always linked with scotopic curves.

Color Receptors in the Frog. In addition to the broad photopic and scotopic curves that we have just discussed, other kinds of narrow curves, sometimes isolated, sometimes coupled with each other, and sometimes coupled to the photopic curve, can be demonstrated. The familiar 'green' curve with a peak at 530 mμ can be found without mixture with any other curve. So also can the 'red' curve with a maximum at 600 mμ. These have already been demonstrated in other eyes that we have taken up.

The newest and most interesting points about the frog eye concern 'yellow' and 'blue' receptors. Sometimes, although not frequently, narrow curves can be isolated whose maxima are clearly at 580 mμ. These are quite distinct from the familiar red receptor at 600 mμ and deserve the name 'yellow.' They almost surely mean that a 'yellow' receptor sometimes uncoupled with any other receptor exists in the frog eye. This receptor, however, is often coupled with a 'blue' receptor (460 mμ), as illustrated in Fig. 74. In fact, it looks as though a 'blue' receptor whenever it appears in this eye is coupled with the 'yellow' receptor, or at least with some other receptor. We shall meet the 'yellow' receptor again in the cat's eye.

In the meantime, there is something quite interesting about the blue receptor of the frog's eye—its special properties of dark adaptation. In Fig. 75 you see a 'blue' receptor coupled with the photopic curve in a record from a single fiber. The graphs of that figure, however, show measurements made at different stages of dark adaptation. In the left-hand graph, the lowest curve is the practically pure photopic curve when the eye has been fully adapted to light. The middle and upper curves show what happens as dark adaptation proceeds: a 'blue' hump gradually emerges and comes to be more prominent than the photopic curve.

The right-hand graph shows the same thing in another way by plotting the sensitivity of the fiber during adaptation to three wave lengths: 650, 500, and 450 mμ. The red wave length, which should excite only the photopic receptor of the two, yields a curve like the typical cone curve of the human dark-

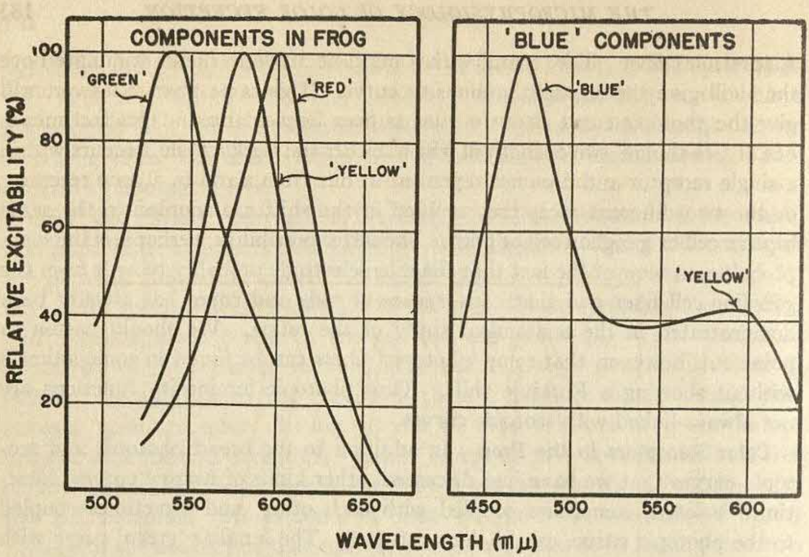

FIG. 74. Components of the retina in the mixed eye of the frog. Peaks in the 'blue,' 'green,' 'red,' and 'yellow' appear in the records. The 'blue' peak, however, is usually coupled with the 'yellow' receptor. (*After Granit.*)

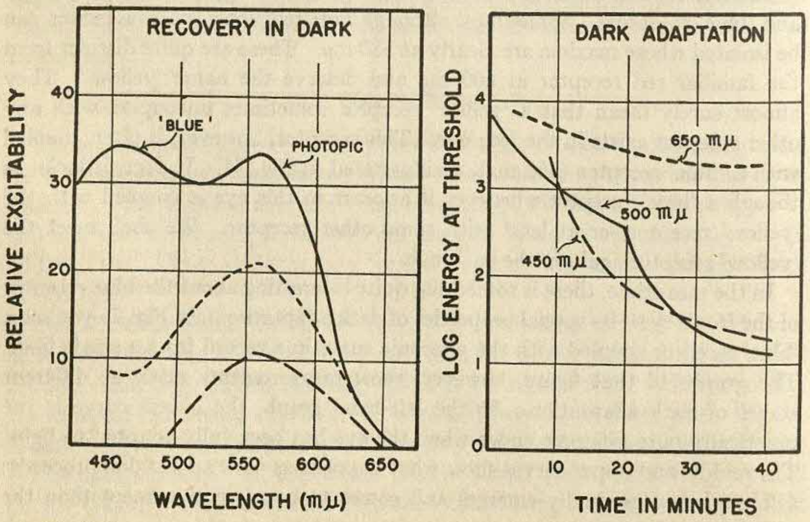

FIG. 75. Recovery of sensitivity in the cells of the frog's retina. The graph on the left shows that the 'blue' part of the curve is much more subject to light adaptation than the 'photopic' part of it but recovers well in the dark. The right-hand graph shows the unusual sensitivity of the eye to 'blue.' At one point in dark adaptation it is more sensitive to blue than to any other wave length. The right-hand graph also illustrates the rod-cone shift in the record of a single cell. (*After Granit.*)

adaptation curve. The 'green' wave length at 500 mμ should stimulate both the photopic receptor and the 'blue' receptor. It gives a curve with two limbs like the cone and rod limbs of the human duplex dark-adaptation curve. Finally, the 'blue' wave length of 450 mμ, stimulating only the 'blue' receptor, yields a curve like the pure-rod limb of a dark adaptation. The interesting thing about these data is that a 'blue' receptor, not a scotopic receptor, is behaving like a rod. We shall come back to this point in a later section.

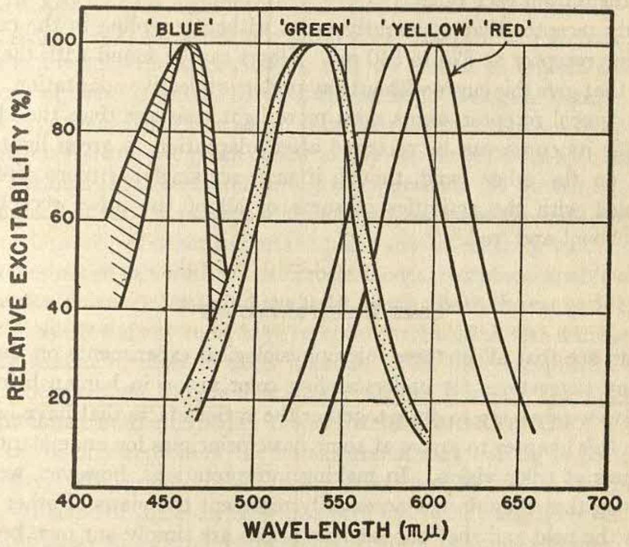

FIG. 76. The components that can be obtained in microelectrode work with the eye of the cat. The 'receptors' seem to be divided into four groups.

'Color' Receptors in the Cat. The last of the mixed eyes to consider is that of the cat (Granit). The microphysiology of this eye brings out several points of interest not seen in the other eyes we have been talking about. Most important is the fact that the specific color receptors of the cat are apparently more frequently coupled to each other than in eyes of 'lower' vertebrate animals. In fact, coupling is more the rule than the exception.

This coupling requires that an additional technique be employed to reveal the color receptors—a technique of selective adaptation by different wave lengths of the spectrum. Most fibers that are picked up before such adaptation give a photopic curve like that already illustrated in Fig. 73. Apparently, however, this supposed photopic curve consists of three or four specific color receptors coupled together. For if the eye is exposed to blue or green adaptation light for several minutes the curve that is then recorded is the typical 'red' curve at 600 mμ (see Fig. 76) that we have met in so many other eyes. Sometimes, instead of a 'red' curve after such selective adaptation, a 'yellow' curve with a peak at 580 mμ turns up. Such 'yellow' receptors, however, appear to be rather rare in the cat's retina. If, on the other hand, the eye is adapted with red or green light, the photopic curve disappears and the familiar 'blue' response curve with a peak at 440 to 460 mμ appears, as you can see in Fig. 76. All three of these receptors, the 'red,' the 'yellow,' and the 'blue,' have been seen in other animals, but in the cat one has to selectively adapt the eye in order to separate them from each other.

The only receptor that apparently exists without coupling in the cat's eye is the green receptor at 520 to 540 mμ. Fibers can be found with the microelectrode that give this curve without any previous selective adaptation. Moreover, the 'green' receptor seems a bit more light resistant than the other receptors, for its curve can be recorded after adaptation to green light. This receptor, on the other hand, though it may act singly, is more often than not coupled with the activities of some or all of the other receptors for 'blue,' 'yellow,' and 'red.'

Some Interpretations

You can see that all of these microphysiological experiments on the retina offer many suggestions for understanding color vision in human beings. In this section we shall try to draw together the various facts that have been presented in this chapter to arrive at some basic principles for understanding the mechanisms of color vision. In making interpretations, however, we should caution you that they do not necessarily represent the views of other investigators in the field and that our interpretations are simply our own best judgment of what the facts to date mean.

Number of Color Receptors. It looks, first of all, as though there are three major groups of receptors present in the eyes of vertebrate animals. Each group is not necessarily present in each animal, but it is present in some animal. One group, the 'blue' group, has maximum sensitivity in the region of 440 to 460 mμ. It is present in the frog, the guinea pig, the cat, and possibly the tortoise. Another group, the 'green' group, has its maximum of sensitivity in the region of 520 to 540 mμ. It is present in the frog, the snake, probably the tortoise, the guinea pig, and the cat. Finally, there is the 'orange' group with maximum sensitivity in the 580- to 620-mμ region of the spectrum. This is present in all the animals named above and, in addition, in the rat.

To say that there are three groups of receptors is not to say that there are only that many individual types of receptors. In fact, it is hard to say just how many different receptors might function in significantly different ways in color vision. For example, is the difference between the 440-mμ 'blue' and the 460-mμ 'blue' receptor significant? Could it be just a matter of experimental error or do receptors in this region of the spectrum naturally vary within this range? We do not know. A similar question can be asked about the 'green' group and the 'orange' group.

In the latter case, there are more grounds for supposing that there is really a difference between the 'yellow' receptor at 580 mμ and the 'red' receptor at 600 mμ. For one thing, the 600-mμ receptor is extremely stable; it appears in practically all animals and its peak seems to hit 600 mμ rather exactly most of the time. Thus when occasionally a receptor at 580 mμ is found in certain animals, it looks like a significantly different one from the 'red' at 600 mμ. Another good reason for accepting the 'yellow' receptor as different is, as we shall see in the subsequent discussion, that we need it to explain some of the phenomena of color as well as some of the microphysiological data.

Let us say, then, that there are at least four distinct types of receptors: the blue of 440 to 460 mμ, the green of 520 to 540 mμ, the yellow of 580, and the red of 600. Perhaps future research will give us grounds for further subdividing these groups, but for the present these four appear to be the 'best bets.'

Rods or Cones? Another important point that is contrary to the duplicity theory comes out of this work with microelectrodes: receptors capable of serving in color vision do not necessarily have to be cones. Both the rat and the guinea pig, which have few if any rods, have receptor mechanisms with narrow spectral sensitivity similar to those in other animals. The 'blue' receptor in the frog, moreover, behaves much more like a rod than like a cone. Thus, despite the classic statement of the duplicity theory, we are forced to raise the question whether the color receptors of the human retina may not be, in part, rods as well as cones. We cannot answer this question now but must wait for future research. If some of the color receptors turn out to be rods, however, the one that is most likely to be a rod is the 'blue' receptor at about 460 mμ. Perhaps others are, too.

PHENOMENA OF COLOR VISION

That completes our survey of the physiological backgrounds of color vision. There are a few additional points which will be brought out in this section. They were left out above in order to avoid saying them twice. Now we shall turn to the psychological phenomena of color vision, attempting to use what we have learned, to see how well we can understand the physiological mechanisms of color vision. This review of the phenomena of color vision will not be complete, nor will it be presented in the conventional order. Instead, what we shall do here is take up the topics according to their order and importance in getting at the physiological basis of color vision.

Photopic Luminosity Functions. Up to this point we have talked as though there were one simple photopic luminosity curve for the human and vertebrate eyes. Actually, there are some important differences in photopic curves—they definitely are not all alike—which are very helpful in piecing together the functions and character of the color receptors.

In the cat's eye, for example, we have already mentioned that there are some fibers picked up by the microelectrode which give photopic luminosity curves but which do not show a Purkinje shift of this curve when the eye is dark-adapted. These fibers, one may surmise, are not connected with any dark-adapting rods but only with cones. Close inspection of the curves (Fig. 77) of these 'pure cone' units reveals that they are not exactly like the typical

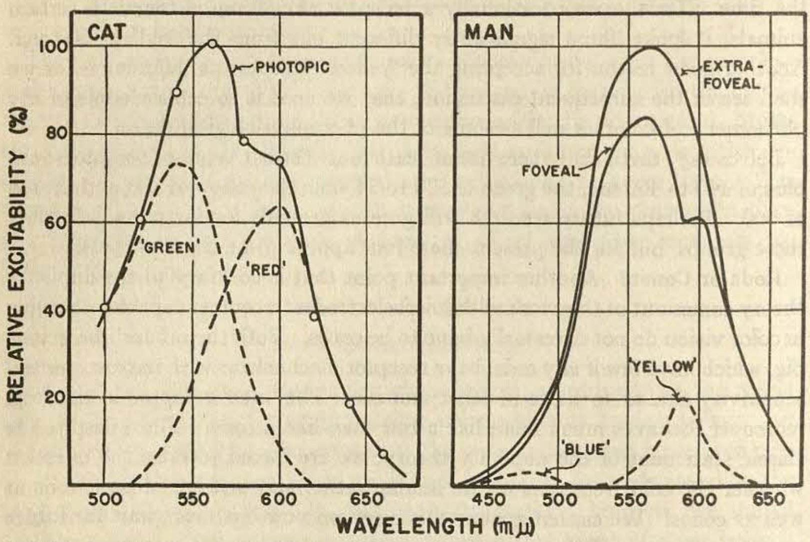

FIG. 77. Analysis of some of the 'photopic' components of the cat's eye into 'red' and 'green' receptors and a comparison of these components with the photopic luminosity curve of the fovea. This kind of curve makes one believe that there are four (or more) color receptors in the human eye. (*After Granit, see pp.* 332 *and* 333.)

photopic curve that we have been seeing in the other work with vertebrate eyes or in the psychological measurements of human photopic vision. Instead, there is a slight depression in the curve between the peak at 560 mμ and a point near 600 mμ. Indeed, it looks as though something that is ordinarily present in photopic curves is missing in this curve.

In man, too, there is a kind of photopic curve that we have not previously mentioned (Wright, Sloan). This curve, seen in Fig. 77, is obtained when all stimulation is confined to the fovea. To get it, investigators have used a very small stimulus patch (20′) on the fovea to make their measurements. The resulting curve also shows a depression, or kink, between 560 and 600 mμ even more prominently than does the cat's curve. In addition, this foveal photopic curve also has something lacking in the blue region of the spectrum, although the difference is small and hard to see. Unfortunately, in the cat's eye, measurements were not made far enough into the blue end of the spectrum to know whether the aberrant photopic curve for the cat is also missing something in the blue.

Composition of Photopic Curves. To make any interpretation of what these differences in photopic curves mean, we must ask a question that up to now we have avoided. Does the photopic curve represent a unique receptor, or is it the composite of several receptors acting together? The classic answer given by color theorists for many years is that the photopic curve is only a composite of individual receptor functions. We now have considerable physiological evidence that this is actually the case. The most conclusive evidence comes from the selective adaptation experiments in cats, which we have already described. You will remember that it was by selective adaptation with particular wave lengths that the photopic curve of the cat was broken down into component receptor curves. Indeed, except for the 'green' receptor, that was how specific receptors in the cat were demonstrated. Some of the points we will come to in a moment also argue for the composite nature of the photopic curve. For the moment, however, let us accept the point and go ahead.

Component Receptors of the Photopic Curve. Believing that the photopic curve is made up of individual receptors provides us with a tool for identifying component receptors in human and animal color vision. In the cat, for example, we can take the pure-cone photopic curve with its depression in the region of 580 mμ and reconstruct it from two receptors already identified in the cat, the 'green' receptor at 530 mμ, and the 'red' one at 600 mμ. The result is given in Fig. 77. There you see that the 'green' receptor is the most dominant component of the pure-cone photopic curve and the 'red' receptor joins with it to make up the whole photopic curve.

For the foveal photopic curve of man, we can make not only this kind of reconstruction but another kind of analysis as well. In the first place, when we compare the foveal photopic curve with the standard photopic curve (extrafoveal) by subtracting one from another, we get an idea of what is missing from the foveal curve (Hartridge). The difference consists of a 'blue' curve and a 'yellow' one. Indeed, within the limits of experimental error, these two curves are identical with curves for the 'blue' and 'yellow' receptors shown by electrophysiological methods. These curves tell us that the 'blue' and 'yellow' receptors are either missing or considerably reduced in number in the foveal photopic curve.

Then, to see what remains in the foveal photopic curve, we can reconstruct it, as we did the cat's, from the curves of individual receptors identified by microelectrode techniques. The result, depicted in Fig. 77, shows that the 'blue' receptor is indeed missing from foveal vision. The 'yellow' receptor, though reduced in number, is still there. The 'green' and 'red' receptors are still present. The process can be checked by going back to the standard luminosity curve—the one without the kink—and reconstructing it out of the component receptor curves. If our assumptions are correct, the final result should give us a picture of the receptors and their proportions that make up the color mechanism in the retina of man.

NORMAL COLOR VISION

We have now established, as well as we can from the available evidence, the basic color receptors of the retina and their characteristic response to different wave lengths of the spectrum. We cannot be dogmatic about the number of receptors and their characteristics, for later research may modify the picture. We can, however, tentatively take the four that have been described as the basis for discussion. With them in mind, let us now run over quickly some of the typical phenomena of color vision in man to see how they tie in with what we have been saying.

Unique Colors. There are thousands of names that have been used to describe various colors. You will realize that if you ever encounter an interior decorator or get lost in a paint shop. All these names, however, are just ways of describing combinations of four relatively unique colors. That was generally accepted long before microelectrode technique identified the color receptors.

What is interesting, moreover, is the fact that the psychologically unique colors correspond rather well with predictions we might make from the curves of Fig. 77. Unique 'yellow' has usually been put at 580 mμ, exactly at the peak of the 'yellow' receptor. Unique 'green' is seen with a wave length of 510 mμ.

At this point the 'green' receptor is almost maximally stimulated, and more important, both the 'yellow' and the 'blue' receptor are excited little if at all. Unique red and blue are a little harder to pin down, but red is seen uniformly above 635 mμ, the point at which the 'yellow' receptor stops responding and leaves only the 'red' receptor still active. And finally, unique blue is seen in the region of 440 to 480 mμ, where the 'blue' receptor responds the most and the 'green' receptor is excited very little. The phenomena of unique colors, therefore, agree rather well with the physiological conception of the four basic receptors.

Complementary Colors. A somewhat similar analysis can be made for complementary colors. It has long been known that red and green are complementary colors and so also are yellow and blue. They are complementary in the sense that when the two colors are mixed they tend to cancel each other out and give a gray or white appearance to the observer. To illustrate complementary colors and their relations to the wave-length spectrum, we can arrange the spectrum in a circle as you see it in Fig. 78. On that circle each color is across from its complementary color. The circle, you will notice, is not a closed one. The colors that lie in the gap are called *extraspectral* because they cannot be produced by any single wave length of the spectrum. They can be made, however, by mixing the two ends of the spectrum in the correct proportions.

And such a color, purple, has its complementary on the opposite side of the circle at a point between yellow and green.

If you study closely the wave lengths in Fig. 78 that are complementary and compare them with the basic receptor curves in Fig. 77, you will see that the two sets of data make sense. The colors that are complementary correspond to the receptors which are being stimulated. You may realize, however, that this complementary relation implies some coupled relationships in the retina between red and green receptors and between yellow and blue receptors. Excitation of red and green receptors mixes to give a gray; so also does excitation of yellow and blue receptors. Such coupling, however, has already turned up in the microphysiological work. In the all-cone eye of the snake, for example, the 'red' and 'green' receptors are very frequently coupled together; 'red' receptors, in fact, always seem to be coupled with 'green' ones. In the frog eye, too, 'blue' receptors were frequently coupled with 'yellow' ones, and so also were 'green' and 'red' receptors. Such coupling of different receptors probably means that they end on the same bipolar or ganglion cells. Moreover, it means that one specific receptor tends to 'inhibit,' or in some way cancel out, the activity of the complementary receptor. We do not know the details of the mechanism, but it is easy to understand in general how coupling of receptors can explain the phenomena of complementary colors.

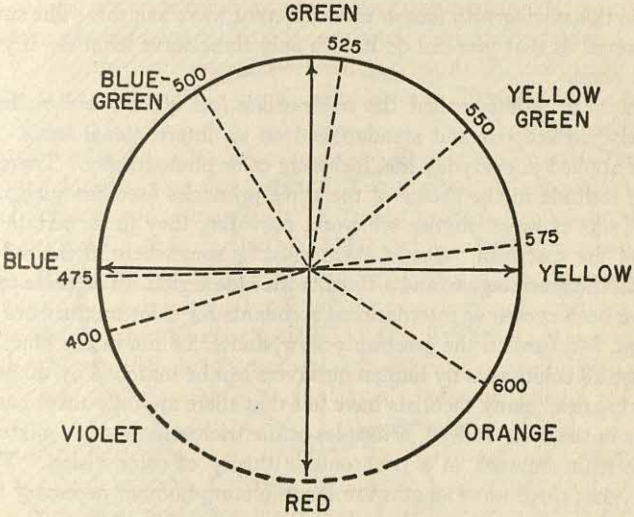

FIG. 78. The visual spectrum and the complementary colors arranged in a circle. The numbers are different wave lengths of the spectrum. Each dashed radius and number stands opposite its complementary wave length. Note that unique red is extraspectral, *i.e.*, unique is a mixture of the long and short wave lengths.

Color Mixture. We have already pointed out that there are only four unique colors in the spectrum and that a color of any other name lies somewhere between these four unique colors. That statement has to do with the naming of colors for different parts of the spectrum. When, however, we come to mix different wave lengths of the spectrum to get any other color or to get a white, we find another interesting set of relations. By mixing a number of different wave lengths in the correct proportions, it is possible to get any color or spectrum that one desires. Obviously, since there are only four unique colors, it is very easy to do this mixing with four or more different wave lengths. The surprising fact, however, is that you can do it with only three wave lengths—if you pick the right ones.

This fact, sometimes called the *trichromatic law of color vision*, has been elaborately worked out and standardized on an international basis. And it is widely applied in everyday life, including color photography. There is considerable latitude in the choice of the three primaries used for such mixture. Different sets of wave lengths will work, providing they lie in certain general regions of the spectrum. One of them must be somewhere in the red region, another in the green region, and a third in the blue region. The three primaries that have been chosen as international standards for color mixture are 700 mμ in the red, 546.1 mμ in the greenish yellow, and 435.8 mμ in the blue.

Because all colors seen by human observers can be matched by mixing these three 'primaries,' many theorists have felt that there are only three basic color receptors in the eye. Indeed, principles of the trichromatic color mixture have been the main bulwark of a trichromatic theory of color vision. The fact, however, that three wave lengths are the minimum number necessary for color mixture in no way argues against there being more than three receptors, and our present physiological evidence points to at least four. Assuming four, rather than three, basic color receptors, it is easy to see why trichromatic mixture works. In particular, one of the three wave lengths used, the one at 546.1, excites both the 'green' receptor and the 'yellow' receptor. The 'greenness' aroused by this stimulus can be reduced by mixing an appropriate amount of red (700 mμ), and the 'yellowness' produced by it can be offset by the appropriate amount of blue (435.8). Thus, because one of the three wave lengths (546.1) stimulates both green and yellow receptors and because there are complementary pairs of green-red and yellow-blue, only two other wave lengths are necessary to make various colors in perception, even though there are probably four or more basic receptors.

Dichromatic Color Mixture. At this point we can return to the special characteristics of the foveal luminosity curve. This, you will remember, seems to indicate that the 'blue' receptor is missing and the 'yellow' receptor reduced in the fovea. Actually, there are considerable data confirming that prediction. In fact, it is relatively easy to demonstrate that people do not report the sensation of blue when the fovea is stimulated with blue light. There are also considerable data to show that the fovea is weak in the perception of yellow, but we will not go into them here (see Hartridge, Willmer).

More interesting and more convincing is the fact that the fovea is dichromatic (Willmer and Wright). That is to say, instead of three wave lengths, only two are necessary in the fovea to match any of the colors seen in the fovea. The two wave lengths only need to be from the two ends of the spectrum, one in the red region (650 mμ) and one in the blue-green region (460 mμ). These two wave lengths, mixed in different proportions, will match the color of anything you can see with your fovea. In terms of the receptor curves of Fig. 77, this means that one wave length stimulates green receptors, the other red receptors.

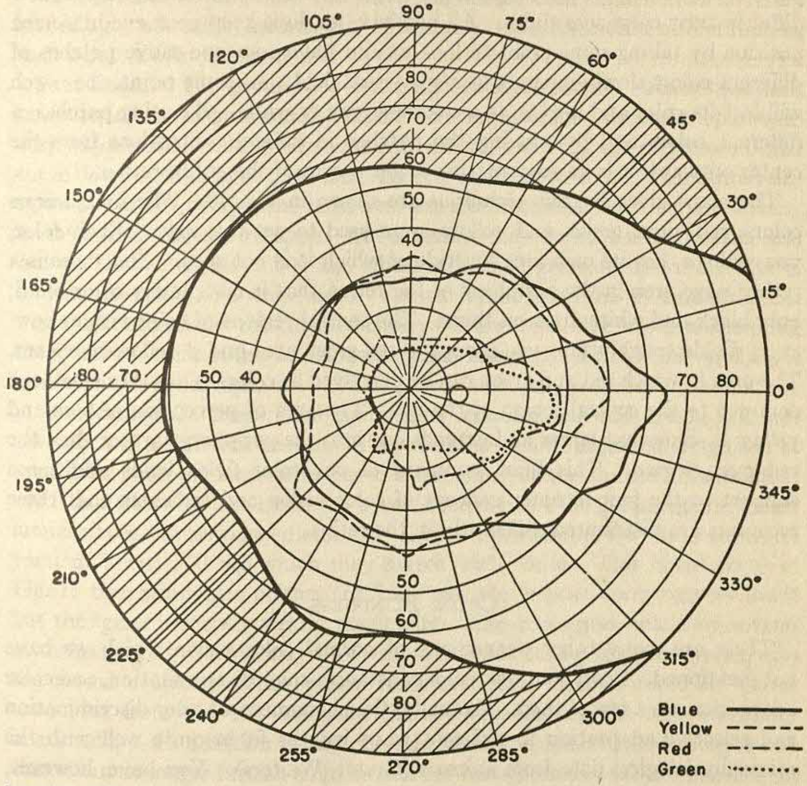

FIG. 79. The color fields of the retina. The map shows the colors that can be seen with indirect vision in different parts of the retina. Nothing at all can be seen in the crosshatched area. Only the grays can be seen outside the lines for the unique colors. Each color has its own color field; blue and yellow have the largest fields, and red and green have relatively small fields in the central region of the retina. [*From E. G. Boring et al. (Eds.). Foundations of psychology. New York: Wiley*, 1948. *P.* 287. *By permission of the publishers.*]

Since these two receptors seem to be the only ones required to make the foveal color matches, it looks as though these receptors are the primary, if not the sole, receptors involved in foveal color vision.

Retinal Color Fields. Next to consider is our ability to see colors in different parts of the retina. It is a simple matter to demonstrate that the retinal regions differ in their color sensitivity. All you have to do is keep your eye in a fixed position by taking some point to look at and have someone move patches of different colors slowly outward in your visual field. At some point, the patch will lose its color and appear as a colorless gray or white. By using patches of different colors and by moving the patches in different directions from the center outward, it is an easy matter to get a map of the entire retina.

The maps given by this technique are shown in Fig. 79. The four unique colors, red, blue, green, and yellow, were used to get this map. Each color, you will see, has its own area, outside of which it is not seen. And there is a rather large area in the periphery of the retina that is completely color-blind; only black and white are seen there. The central regions of color vision, however, divide roughly into two groups, a red-green area and a yellow-blue area. The area in which red and green can be perceived as colors is a rather small one confined to the central region of the eye. The area of perception of blue and yellow is somewhat larger and extends out into the periphery farther than the red-green region. This brief summary of our color fields lends additional support to the four-receptor concept of color vision and indicates that these receptors are distributed differently in the retina.

COLOR BLINDNESS

There are many other phenomena of normal color vision which we have not mentioned. Color contrast, color constancy, color discrimination, and color adaptation are a few of them. Actually, the phenomena of color discrimination and selective adaptation to different wave lengths fit in quite well with the microphysiological data from animals (Granit, Walters). You have, however, had enough examples of some of the basic phenomena to note the most important relations. For further details it would be best to consult one of the numerous works on color vision.

We should not leave color vision, however, without referring briefly to the problem of abnormal or defective color vision—in a word, color blindness. Color defects occur in about 8 per cent of the population, mostly men. They may be either total or partial. It has been conventional to classify color defects in terms of the number of wave lengths required to match all the colors that the person sees. Normal individuals using the whole retina, as we have already seen, are trichromatic, *i.e.*, they require three wave lengths. Color defectives can be classified in the categories described below.

Monochromats. These are completely color-blind people—fortunately quite rare—who need only one wave length to match any other wave length. In other words, all wave lengths look alike, presumably only as grays and blacks. The great majority of color-defective individuals, however, are only partly color-blind and require only two wave lengths for their color matches. They accordingly are called *dichromats*. There are several varieties of dichromats, each with its own special name.

Protonopes. The protonopes are red-green-blind people. Their weakness, however, seems to be primarily in the 'red' receptor, for their photopic luminosity spectrum is shortened at the red end, thus shifting the maximum of the curve downward to about 540 mμ. Indeed, by reconstructing their luminosity curve out of the component receptors, one can conclude that they are lacking in their 'red' 600-mμ receptor. As a result, they confuse reds, greens, and whites. In the region of 500 mμ, where only their green receptors are active, they match colors to a white light. You can understand this by assuming that white light stimulates the complementary 'yellow' and 'blue' receptors, making them 'cancel' each other, and also the green receptor. Thus white light looks 'green' to the protonope.

Deuteranopes. These, like protonopes, confuse red and green, but apparently for a different reason. They certainly have their red receptors, at least their photopic luminosity curve is not shortened in the red. One cannot say either that they are lacking a 'green' receptor, for the green region of their luminosity is not seriously disturbed. Like the protonope, they have a neutral point at about 500 mμ which they match with white. This is the point in Fig. 77 that stimulates neither the 'blue' nor the 'yellow' receptor very much but the 'green' receptor nearly maximally. The best guess, made by several investigators, as to what may be wrong is that something has gone wrong with the neural coupling of the 'green' receptor. This receptor must have been uncoupled from the 'red' receptor, thereby breaking up the complementary relationship. In addition it may have become coupled with rod receptors so that it can no longer furnish a distinction between green and white wave lengths to the brain.

Tritanopes. A third class of dichromat is the *tritanope*, which forms only a small proportion of the color-blind. Tritanopes confuse blue and green and do not see violet and blue as distinct colors. They also have a certain weakness in the yellow region. In fact, they have a neutral or gray point at about 572 mμ, where yellow appears white to them. It turns out, however, that this way of seeing colors is about the same as that of a normal person who uses only his fovea to see with. For this reason one can say that the normal fovea is tritanopic—and thus dichromatic. So far as we know, the photopic luminosity curve of the tritanope is about the same as that of the normal individual. It is possible, however, that the curve shows the same deviations from the normal curve as that for the fovea (see Fig. 77). At present we can diagnose the tritanope as lacking the 'blue' receptor and either lacking or being deficient in the 'yellow' receptor.

Tetartanopes. There is a fourth, but extremely rare, variety of dichromat called the *tetartanope*, who sees the whole spectrum in terms of red and green. Tetartanopes match wave lengths at the short end of the spectrum below 470 mμ, which normally appear violet, with red. Then, between 470 and 580 mμ, normally the transition through blue-green, green, and yellow, they match colors with green. Above 580, they match with red again. It is hard to say what is wrong with their receptor system. Obviously there is some difficulty with their 'yellow' and 'blue.' One possibility is that these receptors have become coupled with the 'red' receptor so that any response in them has the same effect in the brain as stimulating the red receptor. That, at any rate, would explain their peculiar color matching.

Anomalous Trichromats. In addition to these groups of color defectives, there are many people with minor defects who vary considerably in the amount of red and green required to match spectral points, especially yellow. These are called *anomalous trichromats*. It would appear that these people form the transition from normal trichromatic vision to dichromatism. Indeed, it is a question whether we should think of "types" of color blindness as real clear-cut categories. If we think simply of many variations in the presence or absence and in the coupling of the various color receptors, we shall be on safer ground.

General References

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CHAPTER X

HEARING

Our progress in understanding sensory functions depends to a large extent upon our ability to control precisely the physical aspects of stimuli. Only recently have we gained that ability in acoustics. We owe it to the great strides that have been made in electronics, particularly to the development of oscillators and vacuum-tube amplifiers. These instruments enable us to produce known acoustic stimuli, as well as to analyze and record various physiological aspects of hearing. As a consequence, we have made great headway in both the psychology and physiology of hearing in the last twenty years. Although there are still many problems to be solved, hearing is today a field we can survey with some satisfaction.

THE AUDITORY STIMULUS

Sound waves are the stimuli for hearing. There are many sorts of sound waves. Some are simple and relatively pure, like the note of a piano or violin. Some are extremely complex, like speech or the sound of a gun. To give a complete physical description of the nature of all these sounds would get rather complicated, for acoustics, the physical science of sound, is a complicated subject. To serve our purposes here, however, it is necessary to know only a few basic points about sound.

The Nature of Sound. One is that sound is the vibration of an elastic medium. Sound waves are like the vibration of the car or of any solid object, except that they take place in air and fluid media as well. Also, they can be of much higher frequency than the ordinary mechanical vibrations we experience. In air or in water, the sound wave is first a compression of the medium, then an expansion, taking place in the molecules of the medium. The wave of compression and expansion spreads out freely in the medium, progressing at about 1,000 ft. per sec. (760 miles per hour) until it gradually dies out.

Another basic point about sound is that no matter how complex it may be, it can always be analyzed into simple components. This analysis can be made mathematically, if the precise shape of the sound wave is known, by the aid of a formula known as Fourier's theorem. In practice, engineers and research workers have special devices that can be used for performing the analysis. In any event, the simple sound wave, into which all complex waves can be analyzed, is the *sine wave*. Some examples of sine waves are shown in Fig. 80. These waves represent the compression and expansion of the particles of air. The compression gets greater and greater until a peak is reached, then subsides smoothly. But like a pendulum, it overshoots the mark, expanding to a maximum and then returning again toward zero. Every sine wave has two aspects, intensity and frequency, which are what we use to measure and characterize sounds.

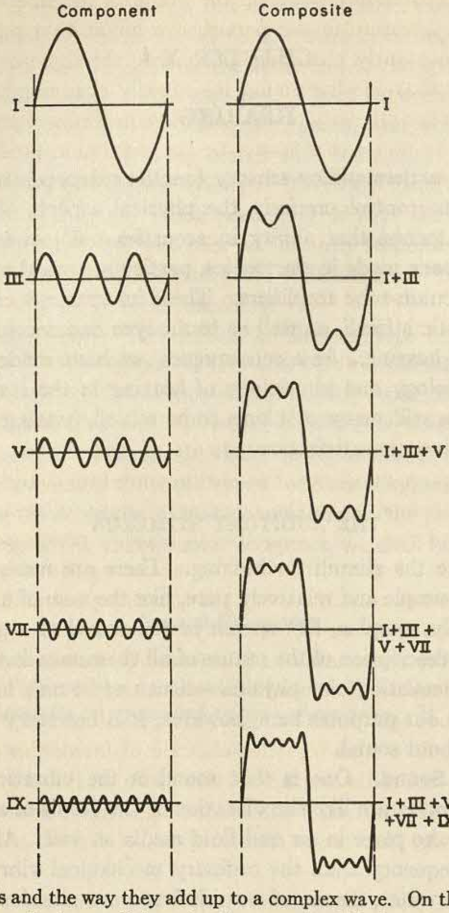

FIG. 80. Sine waves and the way they add up to a complex wave. On the left are sine waves of different frequency, the top one being a low frequency and the bottom one a high frequency. On the right are pictures of complex tones made by adding together different components of pure sine waves. The reverse also works. Any complex sound can be analyzed into some number of sine waves of different intensities. (*From E. G. Boring et al.* (*Eds.*). *Foundations of psychology. New York: Wiley,* 1948. *P.* 316. *By permission of the publishers.*)

Intensity. This corresponds to the magnitude of the swing of the sine wave. Waves with high peaks are very intense; those with small swings are weak. This aspect of a sine wave can be stated in two ways. One is in terms of pressure. The distance from any point on the graph of the sine wave to the base line represents the pressure in the particles of air at that particular instant. The pressure is constantly changing, of course, throughout the duration of the sine wave, for that is what sound is—rapidly changing pressure. If one wanted to measure the intensity of a sound wave in terms of pressure, he would take the peak of the wave; that would be the maximum pressure. There are meters that measure these peaks—they are called sound-pressure meters—and they are used in auditory research.

Energy. Basically, however, we are not interested just in the peak of a sound wave but in the whole wave. So we would like to add up all the various pressures in the sound wave for a given period of time. Such an integration of pressures represents the total energy in the sound wave. And it is energy that acoustical engineers and research workers use as their reference in talking about the intensity of sounds. Pure sine waves, however, always have the same shape—by definition—and it turns out that there is a constant relation between pressure and energy measurements of sine waves. This constant can be used to convert measures of sound pressure into sound energy.

Decibels. That brings us to the question of units of measurement of the intensity of sound waves. For a number of reasons, which we do not need to go into here, we use a logarithmic scale for measuring sound intensities. Such a scale works better not only in acoustical engineering but in understanding the mechanisms of hearing as well. As many of you know, a logarithmic scale goes according to the exponents of a base number, usually taken as 10. So a sound that is 10 times the base would have a value of 1 on a logarithmic scale; one that is 100 times would have a value of 2; one that is 1,000, a value of 3; and so on. The unit of this logarithmic scale of intensities of sound has a name, the *bel*. A bel is the logarithm of a ratio of 10. In most work with hearing, however, this unit of the bel is too big. We need a finer unit. We therefore split the bel into ten parts and speak of *decibels* (db). A decibel is one-tenth of a bel.

Notice one final point about these units of intensity. They are ratios. Seldom are we concerned in hearing about the absolute energy of our stimulus sound waves. We only want to know how much more intense or less intense one sound is than another. We therefore always have some reference intensity. Sometimes we know what it is, sometimes not. Very often the reference intensity is some arbitrary reading, like the number of volts of electricity applied to the loud-speaker we are using in our experiments. It matters little what the reference intensity is, so long as we know what it is. Given a reference intensity, it is a simple matter to describe all the sound stimuli used as some number of decibels above or below this intensity.

Frequency. The second important aspect of a sine wave that must be known to describe it precisely is its frequency. The alternations of pressure that make up sine waves can be very slow, even as little as two or three per second, or they may be rapid alternations of several hundred thousand per second. But a pure sine wave always has a frequency, and we need to know it. The frequencies of sound waves that are involved in human hearing are between 20 and 20,000 cycles per second. Some of the animals have hearing for higher or lower frequencies than this.

With frequency and intensity we can specify all sounds whether they are simple or complex. The complex sounds consist of many different frequencies occurring together, but it is possible to describe them by naming each of the component sine-wave frequencies and giving the intensity of each component. Actually, in everyday life we seldom meet with pure sine waves, although we produce them in a laboratory for precise scientific purposes. The notes of musical instruments are reasonably pure but never entirely so. They are complex sounds in which the various component sine waves are regularly spaced in frequency. The lowest of the components is the *fundamental* tone. Mixed with the fundamental tone, however, are various *harmonic* tones or *overtones*. These are simple multiples, like 2, 3, 4, and so on, of the fundamental tone. The multiple of 2, you may recognize, is the octave in musical terminology. What makes speech and complex noises different from the notes of musical instruments is that the various components of the sound are not regularly arranged in frequency. Instead they consist of a lot of frequencies (sine waves) more or less randomly spaced.

These are the basic points about the physical nature of sound waves. With them in mind we can go on to consider some of the physiological mechanisms of hearing without running into too much difficulty. If more information about sound is desired, it would be well to consult a reference giving a fuller, more technical exposition (Stevens and Davis).

THE AUDITORY SYSTEM

It is only with the greatest difficulty that man has been able to devise instruments for the analysis of sound. Yet the human ear is a mechanism that performs such an analysis with great, although not perfect, precision. Concerned in this analysis are the intricate structures of the external, the middle, and the inner ear, and giving it meaning in human experience are the various auditory centers and pathways of the brain. In this section we shall take up the principal features of these structures. Then in later sections we shall try to see how they are concerned in auditory experience.

The External Ear. What most of us commonly call the ear is to the anatomist only the *pinna* of the external ear. In animals like the dog the pinna is some use, for it can be pointed in different directions to help 'collect' sound waves somewhat more efficiently than we do. For us, however, the pinna is little more than a decoration showing where our real ears are hidden. Aside from the pinna, there are two important parts of the external ear. One is the *external meatus,* the canal that runs from the pinna inward; the other is the *tympanic membrane* located at the end of the external meatus and marking the inner boundary of the external ear. It is through these parts of the external ear that sounds are conducted to the middle and inner ears.

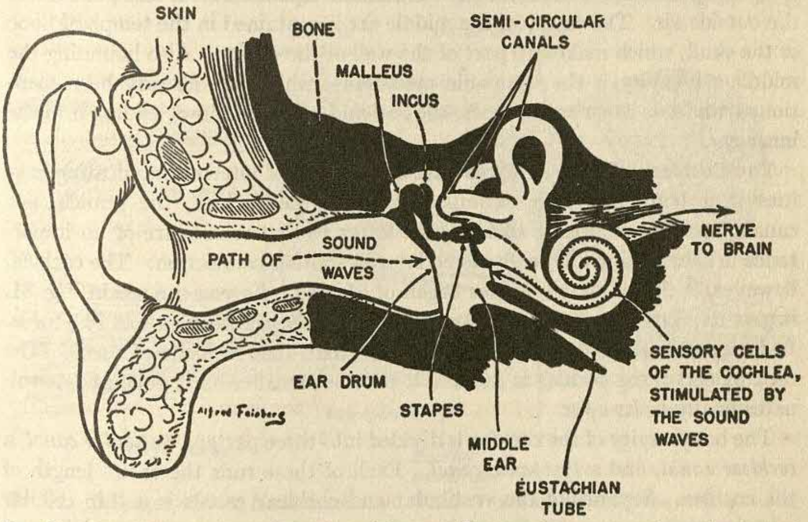

FIG. 81. A somewhat schematic drawing of the ear. The sound waves pass down the channel from the external ear and hit the eardrum (tympanic membrane). There they cause the bones of the middle ear (malleus, incus, and stapes) to vibrate, and one of these bones, the stapes, transmits the waves to the fluid of the cochlea. In the cochlea are sensory cells that are excited by the vibration and start impulses down the auditory nerve to the brain. (*Slightly modified from H. Davis (Ed.). Hearing and deafness. New York: Murray Hill Books, Inc.,* 1947. *P.* 110. *By permission of the publishers.*)

The Middle Ear. Placed obliquely across the end of the external meatus, the tympanic membrane is a cone whose apex points inward (see Fig. 81). Firmly attached to this apex is the *malleus,* one of three ossicles (bones) of the middle ear. Joined by tight ligaments to the malleus is the *incus,* the second of the three ossicles. This articulates in turn with the *stapes,* the third of the middle-ear bones. Finally, the stapes is attached to the oval window (see below) of the inner ear. It is through this series of bones that sounds are conducted from the external to the inner ear.

Associated with the ossicles are two muscles, the *stapedius* and the *tensor tympani.* The latter is attached to the malleus in such a way that when it contracts, tension is put upon the tympanic membrane. The stapedius muscle, on the other hand, is attached to the stapes near its joint with the incus, and its contraction so dampens the movement of the bony stapes that the amplitude of vibration of the stapes is reduced or attenuated.

Surrounding the ossicles of the middle ear is an air-filled cavity. Air pressure in this cavity is ordinarily maintained at the same level as the outside air by means of the *Eustachian tube* connecting it with the mouth cavity—though when you change air pressure rapidly, the *Eustachian* tube sometimes gets clogged up and the middle-ear pressure is not equalized with the pressure of the outside air. The cavity of the middle ear is contained in the temporal bone of the skull, which makes up part of the wall of the cavity. Also bounding the middle-ear cavity is the tympanic membrane, which has already been mentioned, and two other membranes, the *oval* and *round* windows leading into the inner ear.

The Cochlea. The inner ear is part of a system of intercommunicating cavities in a bony labyrinth. Composing it are the cochlea, the semicircular canals, and the vestibular sacs. These latter two structures are of no importance in hearing but will be discussed later in another connection. The cochlea, however, is the primary receptor organ of hearing. As you can see in Fig. 81, it gets its name from its coiled structure. In man, the cochlea has 2¾ turns. In lower animals it may have more or less than that number of turns. The broader end of the cochlea is its *base;* it becomes smaller as it coils and terminates finally in its *apex.*

The bony cavity of the cochlea is divided into three parts: a *vestibular canal*, a *cochlear canal*, and a *tympanic canal.* Each of these runs the entire length of the cochlea. Separating the vestibular and cochlear canals is a thin cellular membrane, known as *Reissner's membrane*, and between the cochlear and tympanic canals is the *basilar membrane.* At the base of the vestibular canal is the *oval window*, to which is attached the stapes of the middle ear, as has already been mentioned. At the base of the tympanic canal is the *round window*, facing into the cavity of the middle ear near the opening of the *Eustachian* tube. All three canals are filled with fluid. Also to be noted is the fact that the vestibular and tympanic canals communicate with each other at the apex of the cochlea through an opening called the *helicotrema.*

The Basilar Membrane. Despite a good deal of study and many theories about the matter, little is actually known of what happens to a sound wave once it has come through the middle ear into the fluid of the cochlea. Probably the best guess about what goes on comes from studies of mechanical models of the ear (Békésy). These present a picture of a *traveling bulge.* The sound wave enters the vestibular canal at the oval window. As it progresses up the canal, the wave of pressure spreads through the membranes and fluids of the cochlea to the basilar membrane between the cochlear and tympanic canals. Thus as the wave moves up the cochlear spiral, a pressure bulge moves up the basilar membrane. Because different parts of the basilar membrane respond differently to different waves, however, all parts of the basilar membrane do not bulge with equal ease. Instead, there is one part of the basilar membrane, depending upon the frequency of the wave, that is maximally bulged. Thus runs the present conception of the action of sound in the cochlea.

Much more certain is the fact that the basilar membrane is the primary receptor organ for hearing. This membrane is composed of tendinous fibers and runs from the base to the apex of the cochlea. Also interesting is the fact that the width of the basilar membrane varies throughout its length, being smallest at the broad base of the cochlea and widest at the narrow apex—just the opposite of what you would expect from looking at the external dimensions of the cochlea.

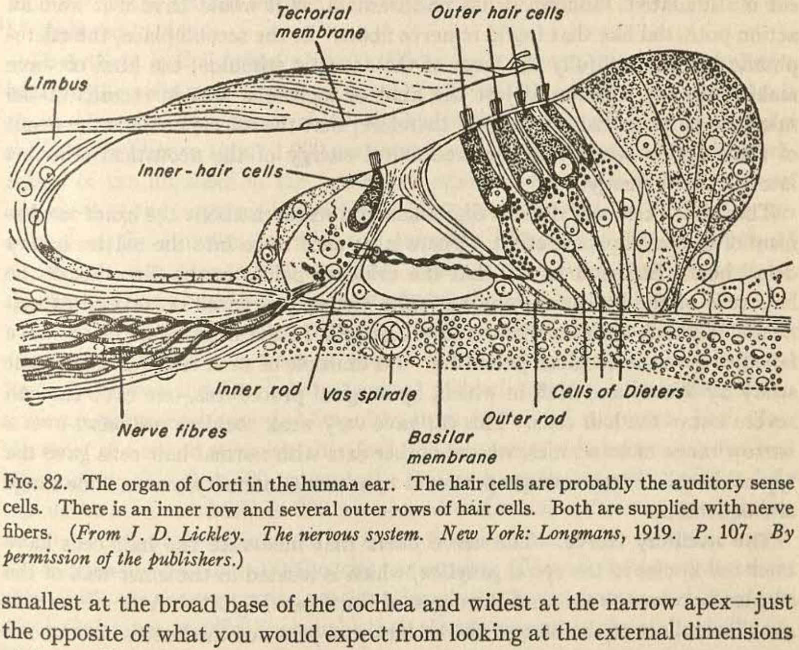

FIG. 82. The organ of Corti in the human ear. The hair cells are probably the auditory sense cells. There is an inner row and several outer rows of hair cells. Both are supplied with nerve fibers. (*From J. D. Lickley. The nervous system. New York: Longmans,* 1919. *P.* 107. *By permission of the publishers.*)

The basilar membrane also contains some fairly complex cell formations facing into the cochlear canal. Of these formations the most important is the *organ of Corti*, situated near the inner edge of the membrane toward the axis of the coil of the cochlea (see Fig. 82). Although there are many supporting cells in the organ of Corti, the most important cells are the *hair cells*, which are arranged in rows of four from the base to the apex. The rows of four, however, are divided by a tunnel and arch into one row of inner hair cells and three outer rows (see Fig. 82). Beneath the hair cells are the endings of the fibers of the VIIIth nerve. Thus the hair cells and the nerve endings make up the primary receptor apparatus.

Cochlear Microphonics. We come now to the first of a series of physiological phenomena of hearing which can be recorded by the appropriate electrical apparatus. This is the so-called *cochlear microphonic*, sometimes called the *Wever-Bray effect* after its discoverers (Wever and Bray). This microphonic is an electrical potential which can be recorded by placing one small electrode on, or within, the bony cochlea and another indifferent electrode elsewhere in the body. The potential is called a microphonic because it clearly arises somehow through the conversion of mechanical energy of the sound stimulus into electrical energy (Wever). In the first place, the microphonic is directly proportional within very wide limits to the intensity of sound with which the ear is stimulated. Indeed, it has no threshold, as it would have if it were an action potential like that found in nerve fibers. In the second place, the microphonic follows faithfully the form of the acoustic stimulus; the kind of wave making up the stimulus is just the kind of wave one sees in records of the microphonic potential. It is clear, therefore, that the microphonic is the result of some action converting the mechanical energy of the acoustical stimulus into electrical energy.

There has been considerable discussion and research about the exact mechanism of the microphonic effect. There is no need to go into the matter in any detail here. Suffice it to say that the evidence points in the direction of the hair cells of the basilar membrane. The evidence is based on several experiments in which animals without any hair cells in the basilar membrane have failed to give the cochlear potentials. An example of such research is a recent study by Wever and Neff in which, by surgical procedures, one cat's ear had severe loss of the hair cells. This cat gave very weak cochlear responses over a narrow range of intensities, whereas other cats with normal hair cells gave the typical cochlear responses proportional to acoustic intensity over a wide range of frequencies.

The Auditory Nerve. The nerve fibers that innervate the hair cells have their cell bodies in the *spiral ganglion*, which is located in the inner wall of the cochlea between its axis and the organ of Corti (see Fig. 81). Axons from this ganglion collect at the base of the cochlea and pass out the bottom of the coil as the auditory branch of the VIIIth nerve. These axons are arranged like a twisted rope; those from the basal quarter of the cochlea form the core of the nerve, and around them twist in one direction the fibers from the apex and in the opposite direction fibers from the middle region of the cochlea (see Stevens and Davis). Just outside the cochlea the auditory branch of the VIIIth nerve is joined by the vestibular branch from the semicircular canal, utricle, and saccule. The two branches divide again, however, just before they reach the medulla. Moreover, the auditory portion itself divides into *dorsal* and *ventral* branches, which end in corresponding nuclei of the medulla. Here are located the cell bodies of second-order auditory neurons.

Auditory Nerve Potentials. The VIIIth nerve, like the cochlea, gives an electrical potential when the ear is stimulated by sound. This potential can be recorded with the appropriate electrodes, amplifiers, and meters. Unlike the cochlear microphonic, however, the auditory nerve potential is an *action potential*. It consists of nerve impulses liberated from neurons by the trigger action of the acoustic stimulus in the cochlea. Most important of the characteristics of the VIIIth nerve action potential is the way in which its frequency is related to the frequency of the sound stimulus. Good synchronization, or 'following,' of the two frequencies holds up to 2,000 or 3,000 cycles per second, depending on the intensity of the stimulus (see Stevens and Davis). Above these frequencies, 'following' is poorer, and above 4,000 cycles, at best, the impulses in the VIIIth nerve are so irregularly spaced that no frequency can be observed in them.

That there is 'following' above 1,000 cycles, however, is of great interest, because the refractory period of fibers of the VIIIth nerve, at its shortest, is about 1 msec. This figure obviously limits the frequency of discharge in a single nerve fiber to about 1,000 per second. In order to account for synchronization of the impulses in the nerve as a whole above 1,000 cycles, we must assume that the impulses in individual fibers are staggered but follow the frequency of the stimulus by *volleys* of impulses (Wever and Bray). Such an assumption has been called the *volley theory*. With it one can account for synchronization above the rate at which individual fibers can follow.

Although 1,000 cycles per second is the theoretical maximum frequency in auditory nerve fibers, it looks as though the actual frequency is considerably less. Galambos and Davis have inserted microelectrodes in the region of the auditory nerve and recorded impulses from individual neurons. Just after the onset of a sound stimulus, they find, the frequency of impulses in individual cells may reach 400 or 500 per second. But with continued stimulation it falls rapidly to a value of 200 or 300 per second and remains there even when the sound is comparatively intense. It looks, therefore, as though volleying begins at considerably less than 1,000 cycles per second. There is, however, one difficulty with the interpretation of the microelectrode experiment. When they did it, Galambos and Davis thought their electrodes were in the auditory nerve. Now it seems likely that the electrodes were actually located in the auditory nucleus of the medulla. If such is the case, the results refer not to the primary neurons of the auditory nerve but to the second-order neurons of the medulla.

Lower Auditory Brain Centers. The second-order neurons, as was mentioned before, lie in the *dorsal* and *ventral cochlear nuclei* of the medulla. Some of the axons of these neurons remain on the same side, but many of them cross the mid-line and make connections with other bulbar nuclei (see Fig. 83). The most important of such nuclei are the *trapezoid body*, located along the mid-line of the lower pons, and the *superior olivary nuclei*, placed more laterally at about the same level. From these nuclei arise third-order neurons which run upward in the *lateral lemniscus* to the *inferior colliculi* of the midbrain. Only a few fibers of the lemniscus pass the colliculi to end in the *medial geniculate body of the thalamus*. Most of those ending in the geniculate come from relay neurons in the colliculi. The final relay station for all fibers of the midbrain auditory tract is the medial geniculate body. Here fibers from the inferior colliculi and all lower levels end.

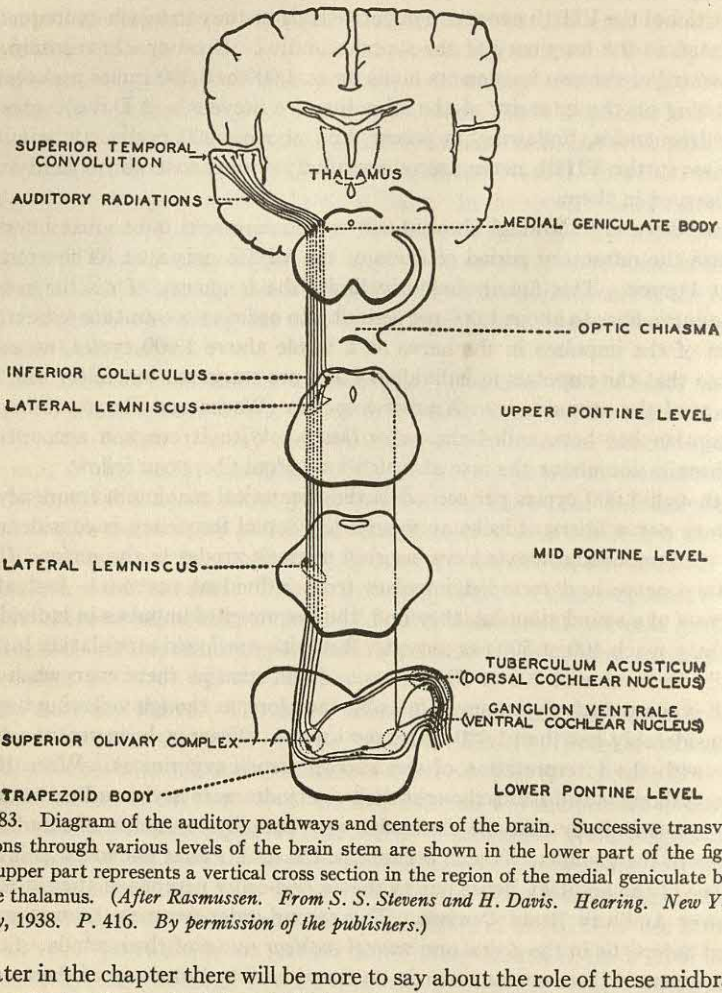

FIG. 83. Diagram of the auditory pathways and centers of the brain. Successive transverse sections through various levels of the brain stem are shown in the lower part of the figure. The upper part represents a vertical cross section in the region of the medial geniculate body of the thalamus. (*After Rasmussen. From S. S. Stevens and H. Davis. Hearing. New York: Wiley,* 1938. *P.* 416. *By permission of the publishers.*)

Later in the chapter there will be more to say about the role of these midbrain centers in hearing. At this point let us simply note the characteristics of the action potentials recorded from them. Electrodes have been placed at different points in the pathways to record these potentials and particularly to see how they correspond with the frequency of the acoustic stimulus (Kemp *et al.*). Recordings from the trapezoid body indicate that the upper limit of following is 2,500 cycles per second, and this can be obtained only with very intense stimuli. A similarly intense stimulus can be 'followed' in the auditory nerve up to or above 3,000 cycles per second. In the third-order neurons of the inferior colliculi, however, the upper limit of following is never more than 1,500 cycles per second and is more typically about 1,000 cycles per second. And in the radiations from the medial geniculate body to the cortex, the synchronization was never more than 500 cycles per second. Perhaps some of these figures are too high—recent experiments make us suspect that (Galambos and Davis, Tunturi). The important point about them, however, is that the degree to which the auditory system can follow the frequency of an acoustic stimulus decreases progressively as we go up the pathways from first-order to third-order neurons.

The Thalamus. The somas of fourth-order neurons of the auditory system are to be found in the medial geniculate body of the thalamus. The axons of these neurons project to the auditory area of the cortex. Thus the medial geniculate body is the auditory relay station to the cortex. In this respect the auditory and visual systems are alike, for the fourth-order neurons of the visual system are in the lateral geniculate body and project to the visual cortex. We shall see in a section below that these thalamic nuclei are only relay nuclei; they have no functions of their own to carry out, other than to get sensory impulses to the cortex.

The Auditory Cortex. There are several ways of telling what part of the cerebral cortex belongs to a sensory system. One of the oldest ways is to trace sensory projections between the sensory nucleus in the thalamus and their termination in the cortex. Very frequently, in using this method, investigators make many small lesions in the cortex and see which ones produce secondary degeneration of the somas in the geniculate bodies. With this method, we have known for a long time the approximate location of the primary auditory areas of the cortex in various animals, including man (see Lashley, Rose).

Another method, the electrical method, has come into use in recent years. It is proving an invaluable tool in mapping areas having auditory functions. This method confirms the existence of primary areas, established by the older anatomical methods. More than that, it reveals the existence of secondary areas which had escaped the anatomical methods. These secondary areas do not receive projections from the geniculate bodies but are associated in some other way with the auditory system. That they are, nevertheless, auditory in function is demonstrated by the fact that they give electrical responses that can be recorded when the animal is presented with acoustic stimuli.

In the electrical method, records are taken from the cortex while the ear is being stimulated. Usually it is best to use brief stimuli, called *clicks*. When the click is sounded, the cortex shows a very complex electrical response. A large positive wave in this response can be used, however, as the index of activity. The stimuli can be applied to the ear in two ways, either by electrical means to the cochlea itself or by the usual sound waves. Both methods give essentially the same results.

In Fig. 84, you see some of the results of using this method with different animals. The first experiments were with cats and employed direct cochlear stimulation (Woolsey and Walzl). They revealed two auditory areas. These areas were subsequently confirmed in similar experiments using ordinary acoustic stimuli (Ades). In the dog, three areas altogether were found, two corresponding to the areas in the cat and a third one in addition (Tunturi). Similarly, there are two auditory areas in the monkey (Bailey *et al.*) and in the chimpanzee (Bailey *et al.*). What the third area is and whether it will be found in animals other than the dog, we do not know.

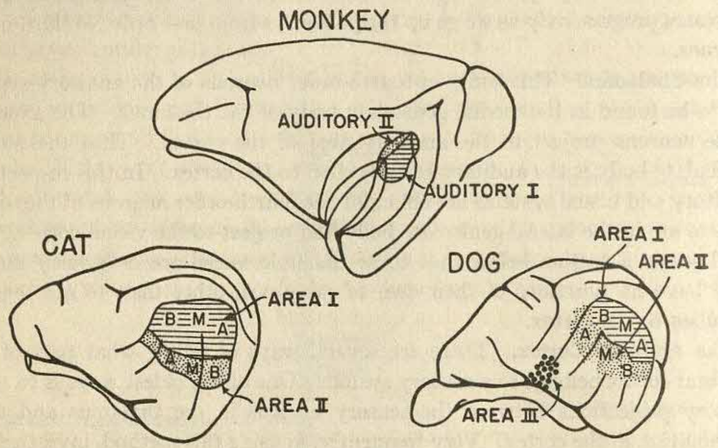

FIG. 84. The auditory areas of the monkey, cat, and dog. All the diagrams are left lateral views of the cortex. Because the auditory area of the monkey is buried partly in the lateral fissure, it is represented as it would be seen with the lateral fissure spread apart. Tonotopic organization is shown by the letters *B*, *M*, and *A*, which stand for basal, middle, and apical parts of the cochlea, respectively. The diagram for the dog is less exact than the others. (*Based on data of Woolsey*, 1947, *and Tunturi*, 1945.)

MECHANISMS OF PITCH

From this point on, we shall take up some of the psychological aspects of hearing and consider the physiological mechanisms underlying them. First, and perhaps the most interesting, is the question of the mechanism for perceiving pitch. You will remember from your study of the experimental psychology of hearing that psychologists distinguish between the intensity and frequency of a tone, on the one hand, and the experiences of loudness and pitch on the other. Intensity and frequency are characteristics of the stimulus; loudness and pitch are the attributes of the auditory sensation. In general, the frequency of sound stimuli is the most important determinant of the pitch sensation, but there is not a one-to-one correlation, and there are factors other than frequency that significantly offset pitch. Our physiological study of the pitch mechanism has not gone much beyond the question of how frequency determines pitch, and that is the problem with which we shall be primarily concerned in this section.

Theories of Pitch. Almost from the beginning of the modern study of hearing, there have been two rival theories of how we appreciate pitch (Rawdon-Smith). One has been called the *telephone theory*, because it supposes that we depend upon the frequency of nerve impulses in the auditory tracts for the perception of pitch. The other theory is known as the *place theory*, for it assumes that it is the place excited in the cochlea and in certain parts of the auditory pathways that determines pitch experience. There are many possible varieties of *place theory*, and it is likely that new ones will be proposed in the future. One type of place theory, the original *resonance theory* of Helmholtz, supposed that the place of stimulation on the cochlea was determined by different resonances of the basilar membrane. From what we know now of the physical characteristics of the basilar membrane, such resonance seems rather unlikely (see Stevens and Davis). Some type of place theory, however, is the theory preferred by modern investigators.

PITCH PERCEPTION AND THE BASILAR MEMBRANE

The most impressive array of evidence for a place theory of pitch comes from the correlation between various aspects of pitch perception and the place of maximal stimulation of the basilar membrane. On the one hand, we have a number of different kinds of evidence that each frequency of an acoustic stimulus excites one part of the basilar membrane more than another. On the other hand, we have many different aspects of pitch perception that seem to follow the same rules as those for excitation in the cochlea. Let us briefly go over some of these facts.

Cochlear Microphonics. We have already pointed out that an acoustic stimulus produces an electrical potential in the cochlea called a *cochlear microphonic*. One can record the microphonic with electrodes placed anywhere on or near the cochlea. Important, however, is the fact that there is always some point on the cochlea that gives a potential of maximum size for each frequency of sound. By finding these points for different frequencies one can construct a map of the cochlea (Culler). One such map for the ear of the guinea pig is given in Fig. 85. There you see that low frequencies give maximal response in the apex of the cochlea, high frequencies in the basal end of the cochlea. Intermediate frequencies have their peaks regularly distributed in between. From these data we are forced to conclude that different frequencies of sound have their greatest effects in different parts of the cochlea. We do not know whether the cochlear microphonic is involved in any way in actual excitation on the basilar membrane—some have thought that the microphonic is produced by the hair cells and it, in turn, is the primary stimulus for the fibers of the auditory nerve (Wever)—or whether it is just an epiphenomenon in which some of the energy of the sound wave is converted into electrical energy. Whichever is the case, the cochlear microphonic shows differential activity of different sound frequencies in different parts of the cochlea.

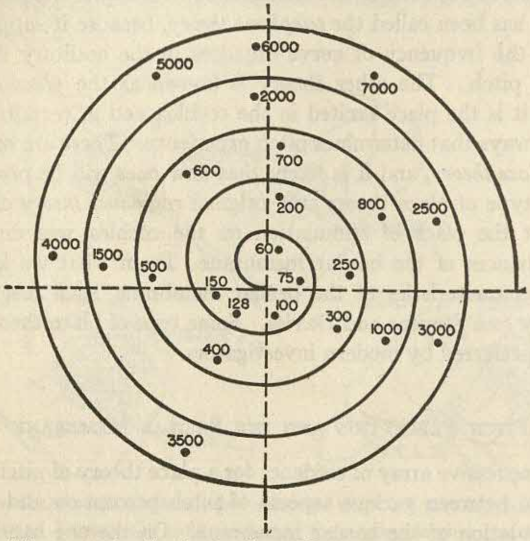

FIG. 85. Map of frequency localization in the cochlea obtained by determining the position in the cochlea for each frequency at which the microphonic potential is maximal. (*After E. A. Culler. An experimental study of tonal localization in the cochlea of the guinea pig, p.* 813. *Ann. Otol., Rhinol., Laryng.*, 1935, **44**, 807–813.)

Exposure Deafness. Later on we shall have something to say about the mechanisms of deafness. At this point we are interested in deafness only because it contributes another bit of evidence on the relation of pitch perception to the differential action of sound frequencies in the cochlea. When the ears of any animal, including man, are stimulated for a long time by a very intense sound, there is some damage to the basilar membrane (Lurie *et al.*, Davis *et al.*). If the sound is a relatively pure sound wave, the damage that follows will occur only in relatively limited parts of the membrane. By stimulating different animals with different frequencies and noting the site of the greatest damage to the membrane, a map of the basilar membrane can be constructed to show where different frequencies stimulate the membrane (Stevens *et al.*). Such a map looks similar to the one constructed from microphonics. In Fig. 86 we see how position of greatest damage corresponds to the frequencies used in stimulation.

Pitch Functions. The interesting thing about the function in Fig. 86 is that it not only describes the sites of cochlear excitation, those of greatest damage and those of the largest microphonics, but it also corresponds to a great variety of perceptual functions of pitch. One such function of pitch is the integral of just noticeable differences (JND's) of pitch discrimination (Stevens *et al.*). If we get the size of the difference in frequency that a human observer can just detect as different in pitch, if we make this measurement at various frequencies, and finally if we "add up" these JND's of pitch, we get a function which corresponds to that in Fig. 86. Another way of getting a pitch function exactly like that in the figure is to have observers make judgments of half pitch, *i.e.*, of tones that sound as though they are just half the pitch of a standard tone. Collating all such judgments into one function gives the same picture as you see in Fig. 86 (Stevens and Volkmann).

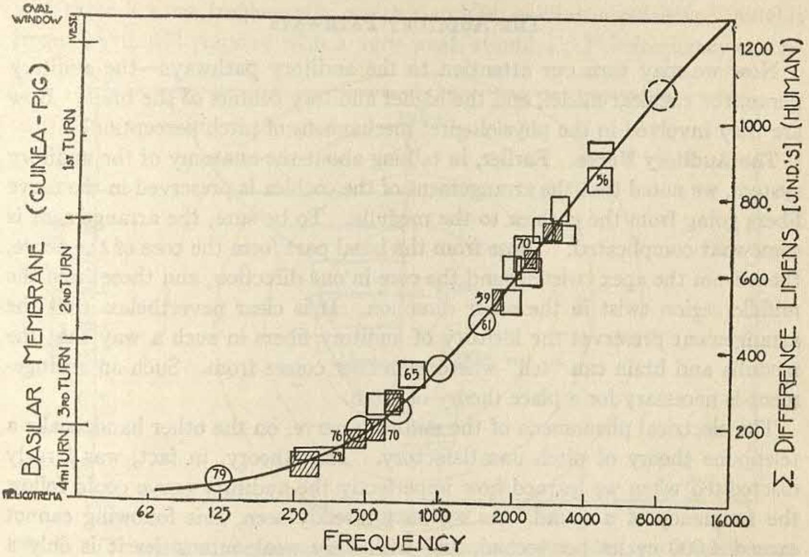

FIG. 86. The relation between position of stimulation on the basilar membrane and pitch perception. The width of the rectangles represents the range of frequencies at which animals suffering from lesions in the cochlea showed loss of auditory sensitivity; the height of the rectangles represents the corresponding region of the basilar membrane showing damage. The centers of the circles represent the centers of the parts of the audiogram showing normal sensitivity and the centers of normal regions in the basilar membrane. The unbroken line is the integration (summation) of the JND's of frequency discrimination. (*From S. S. Stevens et al. The localization of pitch perception on the basilar membrane, p.* 308. *J. gen. Psychol.*, 1935, **13**, 297–315. *By permission of the Journal Press.*)

We have gone over these points hurriedly. When they are all put together, however, they leave us with the conviction that the place of stimulation in the cochlea corresponds extremely well with our perception of pitch. The place of stimulation, to be sure, is not extremely narrow—in fact, the physiological experiments show that any frequency of sound has some effect on a relatively wide region of the cochlea—but it is sufficiently different for various frequencies to provide a good basis for pitch discrimination and pitch perception.

THE AUDITORY PATHWAYS

Now we may turn our attention to the auditory pathways—the auditory nerve, the cochlear nuclei, and the higher auditory centers of the brain. How are they involved in the physiological mechanisms of pitch perception?

The Auditory Nerve. Earlier, in talking about the anatomy of the auditory system, we noted that the arrangement of the cochlea is preserved in the nerve fibers going from the cochlea to the medulla. To be sure, the arrangement is somewhat complicated. Those from the basal part form the core of the nerve, those from the apex twist around the core in one direction, and those from the middle region twist in the other direction. It is clear nevertheless that the arrangement preserves the identity of auditory fibers in such a way that the medulla and brain can "tell" where each fiber comes from. Such an arrangement is necessary for a place theory of pitch.

The electrical phenomena of the auditory nerve, on the other hand, make a telephone theory of pitch unsatisfactory. That theory, in fact, was largely discredited when we learned how imperfectly the auditory nerve could follow the frequency of a sound. As we have already seen, this following cannot exceed 4,000 cycles per second, and with very weak intensities it is only a fraction of this value. Thus the auditory nerve seems to be incapable of acting like a telephone line at high frequencies, yet human and animal observers can hear and discriminate pitch up to more than 16,000 cycles per second. A telephone theory must at best be limited to low frequencies. To hold to it at all would require that we limit it to low frequencies and hold a place theory for high frequencies—a rather unlikely type of physiological mechanism.

The Medulla. It is time to come back to the important study of individual neurons of the auditory system which has already been mentioned (page 205; Galambos and Davis). This study made use of extremely small electrodes, called microelectrodes, approximately the same size as the somas and fibers of neurons. When the study was carried out, its authors believed that they had placed their electrodes in the auditory nerve of the cat. Since that time, however, it has become more and more likely that the microelectrodes were in the cochlear nucleus, not in the auditory nerve (Galambos and Davis). This difficulty comes about because the auditory nerve of the cat is very short and it is not possible to see exactly where the tip of a microelectrode is. Because of this technical difficulty, and because some of the results of the study can only be understood readily on the assumption that they involve second-order neurons of the medulla, we shall here assume that to be the case.

Response Areas. Most important of the characteristics of single units studied by the microelectrode technique is what Galambos and Davis have called *response areas.* Examples of such areas for a few fibers are illustrated in Fig. 87. The response area of a unit includes all those combinations of frequency and intensity that will excite the neuron. Any particular response area shows that there is some frequency to which a unit is maximally sensitive. At this frequency it will respond with a very weak stimulus. This frequency can be used to "name" the unit so that we can speak of a 2,000-cycle unit, a 2,600-cycle unit, and so on. As the intensity of the stimulus is increased, the response areas show that the unit responds to a wider and wider range of frequencies. Thus a 2,000-cycle fiber will respond to frequencies of 300 to about 2,200 cycles per second at very high intensities of stimulation of the ear. It is interesting that when intensity is increased, fibers typically respond to lower and lower frequencies but do not respond to frequencies much higher than the one to which they are maximally sensitive.

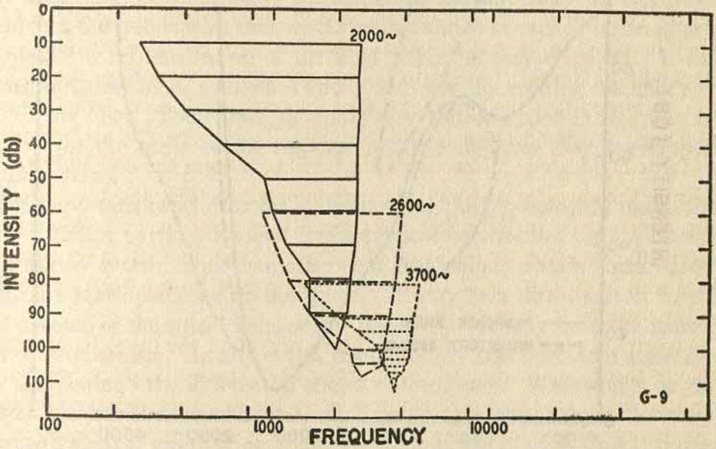

FIG. 87. Thresholds of response at different frequencies for individual, second-order nerve fibers of the auditory nerve. Data for three different fibers are shown: a 2,000-cycle fiber, a 2,600-cycle fiber, and a 3,700-cycle fiber. Each fiber is named by the frequency at which its threshold is lowest. (*After R. Galambos and H. Davis. The response of single auditory-nerve fibers to acoustic stimulation, p.* 45. *J. Neurophysiol.*, 1943, 6, 39–57. *By permission of the authors.*)

Galambos and Davis, by probing with microelectrodes in many cats, have found dozens of fibers with relatively specific response areas like those you see in Fig. 87. In fact, the units seldom respond to a broad band of frequencies except at very high intensities. Even then the response area of a particular unit includes only a portion of the spectrum that the animal can hear. This is the kind of result we expect to find in the auditory system on the basis of a place theory of pitch. It indicates that different neurons in the auditory system are responding to different frequencies of sound stimuli.

Inhibitory Areas. There are other aspects of this study which we will come back to later, but one other fact is especially relevant to the physiological mechanism of pitch (Galambos and Davis). It is the phenomenon of *inhibition* of certain auditory units by acoustic stimuli. This phenomenon, incidentally, argues strongly that the units being studied were second-order neurons of the medulla, for it is only at such a level that one can reasonably expect inhibition to be found. The phenomenon was demonstrated in two different ways. Some of the neurons from which the microelectrodes recorded nerve impulses had their own spontaneous rate of activity. Impulses could be seen when the animal was in complete quiet. Such spontaneously discharging fibers are often found in electrophysiological studies of the nervous system. In this particular case, the neurons often could be made *to stop* firing by sounding a tone in the animal's ear. In Fig. 88 you see two cases of such inhibition. In one, the *inhibitory area* was below the response area; tones of low frequency would inhibit the spontaneous activity of the neuron, while tones of higher frequency (about 1,400 cycles per second) would cause the activity to increase. In the second case the inhibitory area was above the response area; the neuron was most sensitive to a frequency of about 1,400 cycles per second,

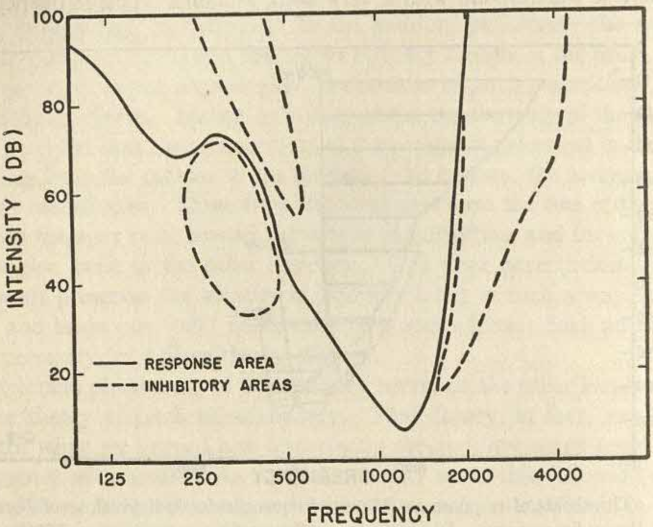

FIG. 88. Composite schematic diagram of inhibitory areas. Probably no single element ever gives results exactly like that in the diagram. It shows, however, that inhibitory areas may occur at frequencies above, below, or the same as those involved in the response area of an element. (*Based on Galambos and Davis*, 1944.)

but its spontaneous activity could be arrested by tones in the neighborhood of 2,000 cycles per second.

A second way in which Galambos and Davis demonstrated inhibition was to sound two tones at once. First they would find the response area for the particular neuron under the microelectrode. Knowing the response area, they could choose a test tone that would excite the fiber. Then they would sound a second tone, changing its frequency from time to time, and find the frequencies that would inhibit the firing of the neuron to the first tone. In this way they could find the frequencies that would inhibit a neuron excited by another tone. In Fig. 88 is an illustration of the kind of results they obtained. It usually turned out that tones somewhat above or below the exciting frequency would inhibit the fiber. Sometimes the inhibitory areas mapped in this way lay to one side or the other of the response areas; sometimes they overlapped the response areas.

The important conclusion for understanding the physiological mechanism of pitch is that a particular sound frequency not only excites certain neurons of the auditory system more than others but also inhibits certain fibers. How the inhibition takes place we do not know. It may be a direct sort of inhibition seen in some of the spinal reflexes (see page 78) or it may be some more complicated mechanism. In any event, the inhibitory effect provides a mechanism for "sharpening" the differential effects of frequency. What starts out in the cochlea as the excitation of a relatively large group of receptors can be narrowed down to a smaller group of neurons by the inhibition of units that also respond otherwise to other frequencies.

The Inferior Colliculi. You have already learned that the frequency of impulses in the tracts ascending from the medulla to the midbrain is between 1,500 and 2,500 cycles per second (Kemp *et al.*). These upper limits of 'following' of an auditory stimulus relegate a telephone theory of hearing to extremely low frequencies of sound. Aside from this fact we know comparatively little of the arrangement of fibers in the ascending lemniscus or its relationship to pitch perception.

At the level of the inferior colliculi of the midbrain, however, we have one study having some bearing on the mechanism of pitch (Coppée). Electrodes were placed in the inferior colliculi and action potentials were recorded during sound stimulation in the rabbit and the cat. The electrodes were not microelectrodes, but they did pick up from relatively limited regions of the colliculi. To obtain the largest possible responses, a 'warble' technique was used. The frequency of a tone was changed up and down rapidly. This technique appears to take advantage of the excitation and inhibition of neurons just described above. At any rate, when an electrode is in any particular place a large potential will appear at certain frequencies and disappear as the tone 'warbles' to another frequency. Changes of the order of 2 to 4 per cent in frequency can be picked up in this way in the potential. These percentages are somewhat larger than the pitch discrimination of a human observer, which may be as little as 0.1 per cent under optimal conditions. They point, however, to a place mechanism for pitch operating even at the level of the inferior colliculus.

The Medial Geniculate Body. At this point it is appropriate to introduce the term *tonotopic organization*, for it will be useful in the rest of this section. The term refers to any physiological arrangement in which different parts correspond to different tonal frequencies of an acoustic stimulus. Tonotopic organization, for example, was seen in the response of the cochlea to different frequencies and, by inference, in the responses of individual neurons of the medulla. Tonotopic organization at different levels of the auditory system is what we should expect to find if a place theory of pitch perception is correct.

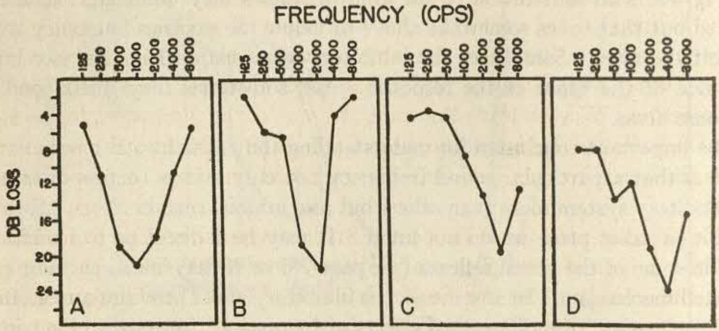

FIG. 89. Losses in auditory sensitivity following localized lesions in the medial geniculate body. *A*, *B*, *C*, and *D* are different subjects (cats) with somewhat different lesions in each case. (*After H. W. Ades et al. Effect of lesions in the medial geniculate bodies upon hearing in the cat, p.* 19. *Amer. J. Physiol.*, 1939, **125**, 15–23.)

Such tonotopic organization is also seen in the medial geniculate body of the thalamus. It has been demonstrated in two ways. One method is to make very small lesions in the medial geniculate body, then to see what effects these lesions have on sensitivity to different frequencies after animals have recovered from the operation (Ades *et al.*). This method employs a special instrument called the *Horsley-Clarke stereotaxic instrument*. This device makes lesions by electrical currents in electrodes thrust deep in the brain.

In Fig. 89 you see the results on four cats subjected to this operation and tested for changes in hearing after operation. The operations produced deficits in auditory sensitivity of as much as 20 decibels, which, as you will see later, is quite significant. Even more interesting is the fact that the deficits were associated with rather restricted frequencies. The frequencies affected depended upon the site of the lesion in the medial geniculate body. Proof was obtained, therefore, of a tonotopic organization in the medial geniculate body just as there is such an organization in the cochlea. It is worth emphasizing, however, that such organization is not absolute but refers only to the maximum of a distribution of neural effects which undoubtedly involves a large portion of the geniculate body.

Falling in line with these results are those of a second method in which action potentials were recorded from different parts of the medial geniculate body (Coakley). In this case, too, a tonotopic organization was found. For each point in the geniculate body from which records were taken there was some frequency of the auditory stimulus that would give the greatest response. Thus we have additional evidence for the tonotopic arrangement at this level of the auditory system that would be required by a place theory of pitch.

Auditory Cortex. You have already learned that it is possible to locate the acoustic areas of the cortex by the techniques of electrical mapping. You know, moreover, that there are always two acoustic areas and sometimes three. What remains to be said about these areas concerns their tonotopic organization. We will leave the third area out of the discussion, for its status is less well defined and is still the subject of research. Of the other two auditory areas, however, we can say that they are laid out in a tonotopic arrangement.

One acoustic area (area I), located in the temporal regions of mammalian brains, has been studied in the cat (Woolsey and Walzl; Ades), the dog (Tunturi), the monkey (Ades and Felder; Bailey *et al.*) and the chimpanzee (Bailey *et al.*). In some cases the stimuli have been electrically applied to the cochlea; in others, they have been pure tones presented to the normal ear. In all cases the maps that are obtained of the area show some tonotopic organization. The largest responses to low tones are in one part of the area and those to high tones are in another part. Indeed, some of the maps are refined enough to show a regular arrangement of the primary area with respect to various frequencies.

The second acoustic area (area II) is similarly arranged tonotopically. The interesting point about it, however, is that its arrangement is the opposite of area I. The two areas, I and II, are located side by side in the cortex, but the end of area I that represents low tone lies beside the part of area II that is specialized for high tones, and vice versa. This reverse pattern of the two areas is something that has been discovered only recently, and we do not yet know what it means.

Unfortunately, we have no behavioral studies to show directly how pitch perception is related to the tonotopic organization of areas I and II. What we should like to have are experiments in which animals are trained to make pitch discriminations and then are subjected to partial lesions in these areas. In this way we could directly relate pitch perception to cortical functions. At the present time we do not have such data. All that we know is that the auditory cortex is tonotopically organized in the way that it should be for pitch perception to depend upon the place of excitation. We know, too, that there are two or more auditory areas in the cortex, but we do not know what their separate roles are.

MECHANISMS OF LOUDNESS

Having reviewed briefly what we know about the physiological mechanisms of pitch perception, we turn now to the problem of loudness. This psychological attribute of auditory sensations, we know, depends primarily on the intensity of sound stimulation. Loudness, however, is markedly affected by the frequency of tones. Moreover, loudness does not always increase in proportion to increases in intensity. In considering the physiological mechanisms of loudness, therefore, we can expect to find some rather complex relations.

PERIPHERAL MECHANISMS

The simplest case of loudness perception is the lower threshold of hearing—the weakest sound of a given frequency that can be heard. The function relating the lower threshold of hearing to frequency is called the *audiogram*. Since this function can be obtained quite easily in animals after training them to respond to the presence or absence of sound, we have much more physiological information about the audiogram than we do about other aspects of loudness. Much of what follows, therefore, will have to do with the audiogram. We shall take up what we know by proceeding in the same order as we did in the previous section—from the ear upward through the auditory system to the cortex.

The Middle Ear. The first structure of physiological importance in loudness perception is the middle ear, particularly the chain of three ossicles that is found there. These bones act somewhat like mechanical amplifiers (see Stevens and Davis). They are arranged in a series of levers so that the vibration impressed on the malleus by the tympanic membrane is amplified in the movement that the stapes delivers to the oval window of the cochlea. The amount of amplification is of the order of 30 db, a considerable factor in increasing our sensitivity to sound as well as the loudness of the sounds we can hear.

Deafness, which is a loss of loudness, comes about in several ways. One way is for something to happen to the middle-ear bones to reduce their efficiency or even to prevent their action in hearing. Certain diseases, such as otitis media, can fill up the middle ear with foreign material and impede the movements of the ossicles. Or hardening and calcifying processes can set in which freeze the three bones together, preventing them from acting like the levers they normally are. In all such cases mild deafness is produced—a deafness that is called *conduction deafness* because it is due to poor conduction of sounds through the middle ear (Davis).

There is another mechanism in the middle ear that has something to do with loudness. This is the *acoustic reflex*. It is the contraction of the *intraaural muscles*, the stapedius and tensor tympani, which are attached to the malleus and stapes, respectively. This reflex occurs in response to loud sounds, particularly of low frequency, and appears to be a protective mechanism provided by nature to see that the inner ear is not injured by too intense sounds. At any rate, it attenuates sounds in their passage through the middle ear (Stevens and Davis, page 267). We learn that fact from an experiment with the guinea pig in which the acoustic reflex could be demolished by the use of light anesthesia. By measuring the cochlear microphonic potential with and without the operation of the acoustic reflex, it was possible to determine the amount by which this reflex attenuated sounds. It turns out that the attenuation is as much as 40 db at a low frequency of 100 cycles per second, and that the attenuation decreases with increasing frequency until it is negligible at frequencies above 2,000 or 3,000 cycles per second.

The Cochlear Microphonics. Moving on now to consider the cochlea, we can see that the audiogram, and perhaps the loudness of intense tones as well, is largely determined in the cochlea. The audiogram of all normal animals and human beings has a characteristic shape. Sensitivity is poor at low frequencies, increases to a maximum in the middle range of frequencies, and falls off again at high frequencies. But although that is the characteristic picture, the region of maximum sensitivity varies somewhat from animal to animal. In man it is 1,000 to 4,000 cycles per second (see Davis); in the dog (Dworkin) and cat (Neff) it is somewhat higher; and in small animals like the rat (Gould and Morgan) and bat (Galambos) it appears to be in the neighborhood of 15,000 to 60,000 cycles per second. Thus audiograms have roughly the same shape, although they may be shifted upward or downward in the frequency spectrum in different animals.

One interesting point about the audiogram is illustrated in Fig. 90. There you see that the shape of the audiogram is matched fairly well by the microphonic potentials that are picked up in or near the cochlea. In taking records of microphonics, we can take some arbitrary value of voltage of the microphonic as a constant response comparable to the auditory threshold. When that has been done for different frequencies of stimulation, the result has sometimes been called the *cochleogram* (Lempert *et al.*). As you see in Fig. 90, it looks roughly like the audiogram. From this fact we may judge that the general relation of auditory sensitivity and loudness to frequency is determined in the cochlea, not in the higher centers of the auditory system.

A word of caution, however, is necessary about the correspondence of the audiogram and the cochlear microphonic responses. We cannot be certain at this time just how close the correspondence is under various conditions. For one thing there are experiments that tell us clearly that the cochlear response may remain normal when part or all of the VIIIth nerve has been cut and when hearing tests show the animal to be completely deaf (Wever and Neff; Guttman and Barrera). The cochlear microphonic is therefore no index of auditory sensitivity when there is something wrong 'upstream' in the auditory system. There are other experiments, too, in which the organ of Corti of the cochlea has been experimentally damaged and the changes in the cochleogram do not correspond precisely with the regions of the cochlea damaged (Lurie *et al.*). All this leads us to believe that the cochleogram may indicate fairly well the relative acoustic stimulation available in the cochlea but not necessarily the excitation of nerve fibers of the auditory nerve or, as is obvious, the sensitivity of higher centers and pathways of the auditory system. This feature of the cochleogram may some day become useful in diagnosing human deafness by showing whether the deafness is peripheral to the cochlea or central to it (see Lempert *et al.*). The technique for such diagnostic purposes has not yet been perfected, however.

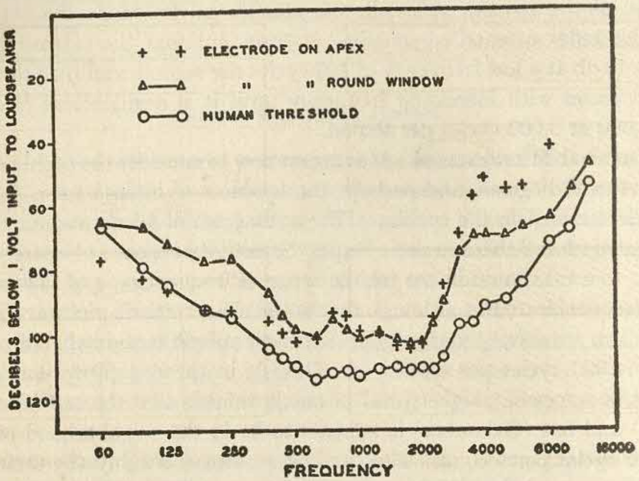

FIG. 90. The cochleogram and the audiogram. Human thresholds of hearing for different tones are compared with 'thresholds' of the cochlear microphonic potential. Since the potential is not all-or-none, the 'thresholds' are worked out by taking some size of potential and seeing what intensity of stimulus is needed to evoke that size of potential. (*From S. S. Stevens et al. The localization of pitch perception on the basilar membrane, p.* 299. *J. gen. Psychol.*, 1935, 13, 297–315. *By permission of the Journal Press.*)

The Organ of Corti. The contribution of the hair cells of the organ of Corti to auditory sensitivity has now been demonstrated in a variety of experiments. Some of these experiments employed very intense tones presented to animals and human beings for a long enough time to cause temporary or permanent damage to the organ of Corti (Lurie *et al.*; Davis *et al.*; Stevens *et al.*). In some of the experiments, small lesions were made with operative techniques in restricted parts of the basilar membrane (Stevens *et al.*). In either case the result was to destroy parts of the organ of Corti. In all cases, too, there was some loss of auditory sensitivity, restricted in general to the region of the basilar membrane destroyed.

The Auditory Nerve. We now have some instructive experiments on the effects of damage to the VIIIth nerve (Wever and Neff; Neff). It is probable that there was also some damage to the cochlear nuclei of the medulla, but the anatomical study of the ears of the animals left no doubt that there had been considerable degeneration of the somas and the fibers supplying the basilar membrane. Perhaps the most remarkable thing about these experiments is the great damage to the auditory nerve that can occur with little or no change in auditory sensitivity. As examples, you see in Fig. 91 the postoperative audiograms of the two cats. One has a completely normal audiogram, the other is normal for the low and middle frequencies but is completely deaf to high tones. Also in Fig. 91 are maps of the proportion of ganglion cells and nerve fibers remaining intact for different parts of the cochlea. Both animals, you will notice, have very few fibers and cells left in the basal and middle parts of the cochlea but have relatively normal innervation at the apical end. There are other cases that you could look at. They would all show the same point fairly clearly. With no innervation of the cochlea at all, complete deafness for the frequencies related to the cochlear region ensues. With relatively few fibers present, however, there can be normal hearing. Apparently, therefore, it is only necessary that a few fibers remain for us to hear the weakest sounds.

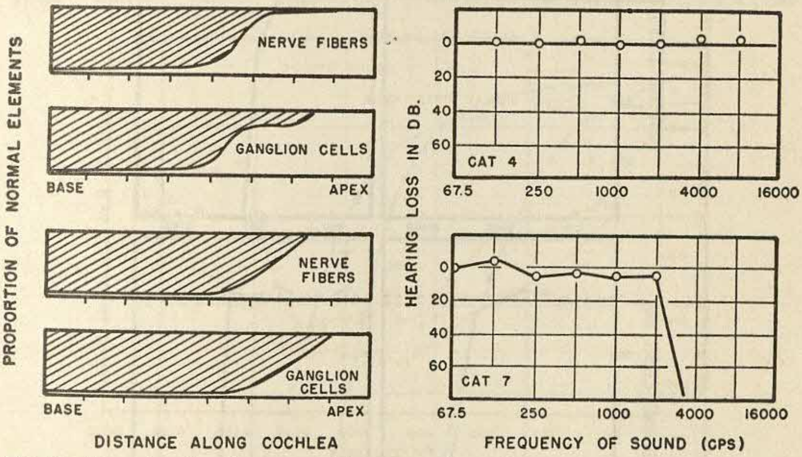

FIG. 91. Examples of audiograms and damage to the cochlea after partial section of VIIIth nerve. The diagrams on the left show roughly the amount of nerve fibers and of ganglion cells destroyed (crosshatched region), and the graphs on the left show the hearing loss (if any) after operation. The upper graphs are for cat 4 and the lower graphs for cat 7. (*Based on the data of Neff, and of Wever and Neff.*)

Nerve Deafness. Clinical otologists have long distinguished two types of deafness (see Davis). One, *conductive deafness*, is caused by some loss in the conduction of sound to the inner ear. Audiograms of people with conductive deafness typically show a rather uniform loss of sensitivity at all frequencies. The other type, called *nerve deafness*, is caused by some damage to the receptor mechanism or the auditory nerve conveying impulses upward to the brain. Cases of nerve deafness typically show either losses of sensitivity in a restricted range of frequencies or losses in the high frequencies. The restricted losses are called *tonal gaps;* the losses in high frequencies are called *high-tone deafness.*

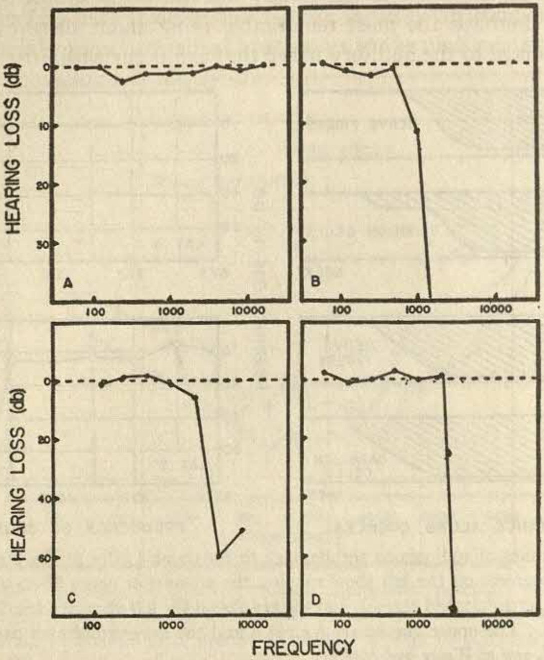

FIG. 92. Examples of changes in the audiogram of cats subjected to partial lesions of the VIIIth nerve. The record in the upper left-hand corner shows no marked loss, but the other three cats have high-tone deafness with little or no loss of hearing for low tones. (*Based on W. D. Neff. The effects of partial section of the auditory nerve. J. comp. physiol. Psychol.,* 1947, 40, 203–215.)

In some recent studies with cats we have an experimental approach to the problem of nerve deafness, particularly high-tone deafness (Neff). The object of the experiment was to see what happens to auditory sensitivity when partial lesions of the VIIIth nerve are made. In Fig. 92 you see the kind of results that were obtained. If the lesion to the nerve was rather mild, just as in the case of mild damage to the organ of Corti (see above), nothing happened to the audiogram. With more severe lesions, however, high-tone deafnesses were produced. Sensitivity in the low frequencies was preserved, but somewhere in the middle range of frequencies sensitivity dropped off rapidly, and above that point the animal was completely deaf to high tones. There were many more animals in the experiment than are illustrated in Fig. 92, but they all gave results agreeing with this general statement.

Just why lesions to the auditory nerve always produced high-tone deafness, if they affected hearing at all, is not completely clear. The experimenter (Neff) deliberately attempted to vary his lesions in order to damage different combinations of auditory fibers. Apparently, however, he did not succeed, for a postoperative study of his animals indicated that fibers serving the "high-tone" end of the cochlea (base) were usually the ones most severely affected by the operation (Wever and Neff). That much is quite clear. Why it happened is not. There is the possibility, however, just as in the experiments with individual nerve fibers, that the lesions were not made in the auditory nerve itself but rather in the cochlear nucleus where the nerve fibers end. If the part of the cochlear nucleus concerned with high tones was always damaged in these experiments, it would explain the results.

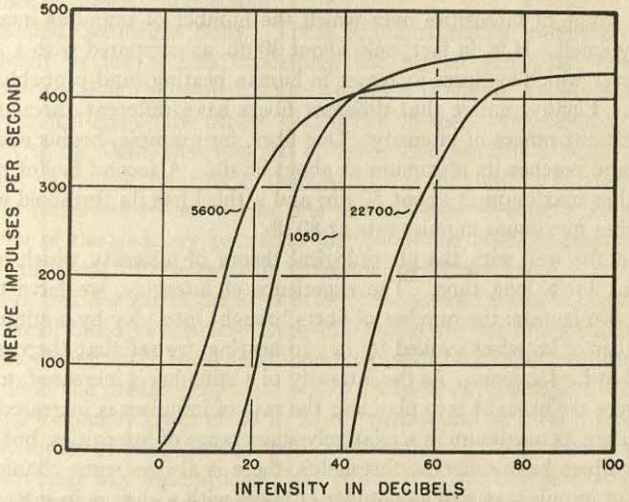

FIG. 93. The frequency of impulses in individual elements of the auditory system. One element responds maximally at 5,600 cycles per second, another at 1,050 cycles, and another at 22,700 cycles. These are just three examples. (*After Galambos and Davis*, 1943.)

Individual Fibers. Further light is shed on the mechanisms of auditory sensitivity and loudness by experiments with individual neurons (Galambos and Davis). As we said before, it is a question whether the individual elements were those of the auditory nerve or second-order neurons of the cochlear nucleus. For present purposes, it does not matter. Wherever these elements are located, it is instructive to see how they are affected by the intensity of tones used to stimulate animals (cats) during the recording of impulses from the units. Figure 93 shows the kind of results that were obtained.

In this graph, notice first of all that the number of impulses given by a neuron increases with the intensity. At very weak intensities there are no impulses at all. Increasing the intensity increases the number of impulses up to a maximum of about 400 impulses per second. Not shown in Fig. 93, however, is the fact that this rate can be maintained only for a fraction of a second after the onset of a sound, and neurons quickly adapt so that the rate of impulses decreases to about 150 or 200 per second. Second, in Fig. 93, you see that the range of intensities over which the number of impulses increases is relatively small. It is, in fact, only about 30 db, as compared with a range of 100 db over which loudness increases in human hearing (and probably also in the cat). Finally, notice that different fibers have different thresholds and cover different ranges of intensity. One fiber, for example, begins responding at 0 db and reaches its maximum at about 35 db. A second begins at 15 db and reaches maximum at about 50 db; and a third has its threshold at 42 db and reaches maximum impulse rate at 80 db.

All this fits well with the physiological theory of intensity which has been prominent for a long time. The experience of intensity, we have thought, rests on two factors: the number of fibers brought into play by a stimulus and the number of impulses evoked by it. In hearing, we see that there is such a mechanism for loudness. As the intensity of a stimulus is increased, more and more fibers are brought into play and the rate of impulses is increased. Each fiber reaches its maximum in a relatively short range of intensities, but because different fibers have different thresholds, there is always some change in the number of impulses as well as number of fibers with a change in intensity.

Brain Mechanisms of Loudness

So much for the facts of how the cochlea and lower auditory pathways work with respect to acoustic intensity. The rest of our story about loudness has to do with the role of the higher centers of the brain. So far no one has conducted any studies in which we can find out how the auditory system works in the discrimination of loudness—*i.e.*, the discrimination of differences in the intensities of sounds. All that we have are experiments on the absolute threshold of sensitivity of hearing. It is these that we shall take up briefly now.

The Auditory Cortex. There are three groups of studies in which effects of removal of the auditory areas of the cortex have been measured. They give somewhat different results. In one there seemed to be a loss of 10 db or more in the absolute threshold after removal of all auditory cortex (Brogden *et al.*). In a second study there were losses of the order of 10 to 70 db immediately after the operation, but with the passage of time, auditory thresholds returned almost to normal (Girden). The permanent losses varied between 3 and 10 db. In a third study the permanent losses due to removal of auditory cortices were practically negligible (Kryter and Ades). Putting the picture together from these three studies, it looks as though there may be large temporary losses but small permanent losses following cortical lesions of the auditory system. Why the short-term losses, we do not know. We may conclude, however, with respect to permanent function, that the auditory cortex does not play a very significant role in auditory sensitivity or in loudness. The lower centers must be the ones of primary importance.

The Medial Geniculate Body. There is, unfortunately, even more serious disagreement in the studies concerning the medial geniculate body. All indications are that the medial geniculate body is simply a relay station for auditory projections to the cortex, that it has no special functions of its own. We might think, then, that removal of the medial geniculate would have no more effect on auditory sensitivity than removal of the auditory cortices. That, in fact, is what was found in two cats of one study who were subjected to destruction of the auditory pathways just below the medial geniculate body (Kryter and Ades). These two cats showed no significant losses. On the other hand, there was one cat in the same study that showed a loss of about 12 db, which is small but appreciable. These differences are not so disturbing, however, as those mentioned earlier and found in cases where small localized lesions were made in the medial geniculate bodies (Ades *et al.*, see page 216). Here, interestingly enough, losses of 20 to 25 db were found at certain frequencies when only a part of the geniculate body was destroyed. Only further research can make it clear why these studies disagree and thus just how much the medial geniculate bodies contribute to auditory sensitivity.

The Inferior Colliculus. To date we have only one experiment to tell us what the auditory midbrain center, the inferior colliculus, contributes to sensitivity and loudness. In this experiment there were two approaches to the problem (Kryter and Ades). One was to remove the inferior colliculi on both sides without interfering with the rest of the auditory system. The result was a loss of about 15 db, on the average, in auditory sensitivity. This is appreciable but not great. The second approach was to remove the inferior colliculi in combination with the medial geniculate body or the auditory cortex, or both. In either case the loss was about 40 to 50 db. It made little difference whether the medial geniculate was removed along with the auditory cortex and inferior colliculi; the results were the same, about 40 db loss.

Now to make a short summary of these experiments on the higher auditory centers. The auditory cortex makes only a slight, perhaps insignificant, contribution to auditory sensitivity. Perhaps the medial geniculate body makes a little more difference, but we cannot be sure. With the entire auditory system above the midbrain destroyed, including the inferior colliculi, the geniculates, and the auditory cortices, mild deafness of 40 db or so ensues.

This latter fact means that the lower centers of the brain stem in the medulla are the most important contributors to auditory sensitivity, for after the loss of 40 db there is still a range of more than 60 db of hearing left.

MECHANISMS OF LOCALIZATION

There is another aspect of auditory function on which there is some physiological information. This is our ability to localize the direction and to some extent the distance of sounds in space. Both human beings and animals can perform such auditory localizations with a high degree of accuracy, with the exception that sounds in the median plane of the head are subject to some confusion. Obviously such auditory localization is a binaural phenomenon. It must depend upon differences in stimulation of the two ears. For many years now we have recognized that there are three different types of binaural cues that may serve us in localizing sounds.

Intensity. If two sounds, differing only in intensity, separately stimulate the two ears, it may be demonstrated that intensity differences in the two ears will determine to which side a sound is localized (Steinberg and Snow). The source of the sound, which is imaginary in this case, is judged to be on the side of the greater intensity. In the case of actual sounds, binaural intensity differences cannot be very important at low frequencies because there are not very great differences in the stimulation of the two ears at these frequencies. Physical measurements, however, assure us that at high frequencies the head throws a significant "sound shadow." Above 5,000 cycles per second, the difference in the stimulation of the two ears may be as much as 30 db. Thus the use of an intensity cue in localization at high frequencies reduces in principle to a binaural loudness discrimination. We have already discussed the physiology of loudness and have nothing new to add here.

Phase. This is the second of three possible cues to auditory localization. A sound coming from one side or the other of the head will reach one ear in a slightly different phase from the other ear. There are three factors involved in the mechanism of reacting to such phase differences. One is purely physical. It is the width of the head. The phase difference between the two ears is determined by the frequency of the sound, the speed of sound (which for all practical purposes is constant), and the width of the head. Physical calculations show that phase should not serve as a reliable cue to localization for frequencies above about 800 to 1,000 cycles per second. Because of the width of the head, above this frequency, phase differences would be more than 180 deg. and the observer would not know which ear was leading and which was lagging.

The other two factors relevant to phase cues in localization are physiological. One is the question of the phase in which excitation takes place in the cochlea. For phase to serve as a cue, it is necessary that the impulses in the auditory nerve arise at a certain phase of the auditory stimulus. We have some physiological data on that point, derived from the microelectrode experiments of Galambos and Davis. They recorded the microphonic potential of the cochlea at the same time as they picked up impulses in individual units of the auditory tract. Thus they were able to correlate the phase of the stimulus in the cochlea with the time of origin of nervous impulses. They found that auditory impulses always arose in a definite part of the sound cycle. In Fig. 94 you see such a record illustrated. There the impulses consistently arise in one part of the cycle. The variability, in fact, in time of arousal of impulses is about 0.25 msec. From this figure one might predict that binaural phase cues could be useful up to 3,000 or 4,000 cycles per second.

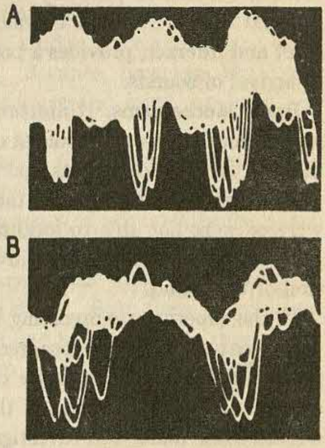

FIG. 94. Nerve responses occurring in a constant phase of the cochlear microphonic waves. Each record is a photograph of many sweeps on the face of a cathode ray tube. The white dips downward are responses of an individual nerve element, and the heavy white waves are the cochlear microphonics. Record *A* is for a stimulus of 1,050 cycles per second, and record *B* is for a sound of 550 cycles per second. (*From R. Galambos and H. Davis. The response of single auditory nerve fibers to acoustic stimulation, p. 51. J. Neurophysiol., 1943, 6, 39–58. By permission of Charles C Thomas, publisher.*)

The final physiological factor limiting the use of phase cues in localization is the degree to which neurons of the auditory tracts can follow, the frequency of the sound stimulus. We have already been over this point (see page 204). We have seen that as well as we can record it, the limit of such synchronization decreases as we go up the auditory tract and probably is less than 500 to 1,000 cycles per second at the cortex. It is interesting that the latest data on the discrimination of phase differences in human observers places an upper limit of about 800 cycles per second on such discrimination (Garner). Thus the physiological, physical, and psychological data on this point all fit together rather well.

Time. The third aspect of sounds that has been regarded traditionally as a cue for sound localization is time of arrival of sounds at the two ears. There is one physiological experiment that gives us some hint as to what and where the physiological mechanism might be for discriminating binaural differences in time of arrival. It is a study of electrical responses in the medial geniculate body and the auditory cortex when the same ear or two ears are stimulated in succession (Tunturi). In this case the technique was to place stimulating electrodes in symmetrical positions on the two cochlea.

By varying the time between successive 'click' stimuli, it was possible to measure a period of unresponsiveness in the geniculate bodies and the cortex, during which a second 'click' would not produce any response. This period was 20 to 100 msec., depending upon various experimental conditions. The important point is that the period was the same for monaural as it was for successive binaural stimulation. From this fact it is possible to conclude that there is a common pathway used by the two ears in getting messages to the cerebral cortex. Such a common pathway, where stimuli from the ears can meet and interact, provides a possible basis for binaural discrimination of time of arrival of sounds.

Brain Mechanisms. Unfortunately there are few experiments, and as yet no satisfactory ones, on the role of different auditory centers of the brain in localization. In the experiments that we have, we do not know whether phase, time, or intensity was important in the localization. We only know that the animals were or were not able to localize. Two techniques have been employed, one involving learning, the other involving reflex turning of the head in the direction of the sound.

In the experiments involving learned discriminations, we have disagreement —or what seems to be disagreement—in results. In the rat it has been reported that animals are quite capable of making auditory localizations after complete bilateral removal of the auditory cortex (Pennington). In the cat, on the other hand, one investigator has failed to get cats to learn to make a discrimination based on auditory localization (Neff). It is possible that the disagreement is due to differences or difficulties in training techniques or to imperfect knowledge of the auditory areas to be removed. Or it is possible that there are subtle deficiencies in localization in the absence of the auditory cortex that show up only under certain conditions. Only future research will tell.

Reflex methods of testing auditory localization give us still another story (Bromiley). Many animals lacking a large part of their brain will turn their head reflexly in the direction of a scratching sound. This may be used to test auditory localization and, in fact, to measure its accuracy. Such a method indicates that animals—at least cats—lacking all of their cortex, all of their thalamus, and some of the midbrain structures are still quite capable of localizing sounds. In other words, decerebrate animals with none of the auditory centers above the midbrain have reflex localization of the direction of sounds.

It will be interesting to see what future research can tell us about the complete mechanism of auditory localization.

COMMENT

That concludes this summary of the physiological mechanisms of hearing. As you see, there are many problems that have not yet been solved. The progress made in recent years, however, is gratifying.

There are a number of problems in hearing that we have not touched upon in this chapter either because of lack of space or because of insufficient information about the problem. For example, there has been a great deal of excellent work in the field of auditory discrimination that has some bearing on the physiological mechanisms of hearing, including studies of the masking of tones by noises and other tones (Stevens and Davis) and the perception of pulses and complex noises (Garner). The authors of these studies have given some clear and convincing physiological interpretations. Because, however, the work did not make direct use of physiological techniques and facts, we have not considered it here.

There are some subjective phenomena of hearing that can be understood in terms of our present knowledge of the auditory system. One is the phenomenon of aural beats, heard by an observer when two tones of very nearly the same frequency are sounded together (see Stevens and Davis). Another is the experience of the overtones or harmonics of a fundamental tone when these overtones are not actually present in the stimulus (Wever *et al.*). Both these phenomena are known to arise in the cochlea. We have not had time to go into them here, but the interested reader may delve into them by looking up the indicated references.

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CHAPTER XI

THE SKIN SENSES

We have now covered the senses of smell, taste, vision, and hearing. There are still some important senses left—those of the skin, of the muscles and joints, and of the nonauditory labyrinth. Because the labyrinthine receptors have so much to do with reflexes and so little to do directly with sensory experience, we shall let them go until we get to the subject of reflexes and posture. The senses remaining make up one interlinked system—somesthesis. The system, however, is so complex and presents such varied problems that we cannot cover it all in one chapter. The present chapter, therefore, will deal only with the receptors and sensory functions of the skin. The chapter that follows will take up the muscle sense and the central somesthetic mechanisms. This way of dealing with the somesthetic system is somewhat artificial but is convenient for our purposes here.

THE SKIN AND ITS RECEPTORS

As you might easily guess, the first basic question about our skin senses is, How many are there? Or, put another way, what are the fundamental qualities of sensation arising from the skin? The second and closely related question is, What receptors are responsible for the qualities of sensation? Or, if there are not specific receptors for each quality, what are the receptor mechanisms for conveying quality to the central nervous system? It is impossible to separate these questions clearly, for evidence concerning one question also throws light on the other. You should therefore bear them both in mind as the discussion goes along.

The Basic Sensory Qualities

To begin the attack on these problems, let us first resort to our everyday experience. What kinds of experiences do people commonly report when they are touched, scratched, pricked, or otherwise stimulated through their skins? If we count them all, there are quite a number of such experiences. There is warmth and cold, tickle and itch, quick pricking pains and duller, longer lasting pains, and there are sensations of pressure or touch and of vibration. There are many words in our vocabulary to describe these various sensations, but most people would probably agree that they would simmer down to this basic list. Now let us see how these experiences are, or are not, related to each other.

Punctate Sensitivity. The first step, in modern times, toward the classification of basic cutaneous qualities was the discovery of the punctate sensitivity of the skin. This discovery was made back in 1883 and 1884 (see Boring). It was observed that the skin was not uniformly sensitive to all sorts of stimuli but had spots that were very sensitive surrounded by areas of relatively poor sensitivity. If, for example, a warm rod is touched to various points on the back of your hand, there are some points where you can feel it as warm, others where it is just something being touched to your hand. This phenomenon is called punctate sensitivity of the skin.

Differential Mapping. The phenomenon has many implications that have fostered research. One of them is the possibility of finding out which are the fundamental qualities of cutaneous sensation. The idea is simple. By making maps of punctate sensitivity for different kinds of stimuli, one can see which ones are alike and which are unalike. For example, take a stylus that is slightly cooler than the normal skin temperature and make a map of any convenient area of the skin, finding the points where the observer can feel 'cold.' Then take a stylus slightly warmer than the skin temperature and remap the area to find the points at which the observer can feel 'warmth.' If these two maps are not the same—if the points for 'cold' are different from those for 'warmth'—then it seems quite clear that the 'cold' sense and the 'warmth' sense are really different senses.

The Basic Qualities. That, in fact, is exactly the result and the conclusion of making maps for cold and warm stimuli. Many research workers have proved it over and over again (see Stone and Jenkins). We therefore can be quite sure that warmth and cold are different. There is a similar story for 'pain' and for 'touch' (Jenkins and Stone). If you take a needle and with light pricks map the points in an area of the skin at which there is a report of pain, then make a similar map for reports of 'touch' when a stylus is placed lightly on the skin, the two maps are different enough to convince you that the two senses are different. You could also compare the maps for pain or for touch with those for cold or warmth and find that they are different. Thus we can be sure that there are at least four different basic qualities of cutaneous sensation: touch, pain, cold, and warmth.

The Derived Qualities. The next question is whether there are any more than these four fundamental qualities. There have been a good many experiments, and at times some controversies, about that question. We are beginning, however, to be fairly sure of the answer to it. It looks as though such experiences as vibration, itch, and tickle are derivations or variations of the four fundamental qualities.

Consider first the experience of vibration. There were some investigators who thought that we must be endowed with a separate sense and separate receptors for appreciating vibration. There may still be some who think so, but the evidence is now marshaled against it (Geldard). There are several kinds of evidence, but one is the clearest and easiest to understand. With the appropriate sort of mechanical vibrator in hand, one can find the threshold of vibration—the amount of movement of the vibrator that can be detected as vibration—for different spots in some region of the skin. As in other similar cases, there are peaks and valleys of sensitivity. This map can be compared with one obtained for touch alone—the points where a small stylus of a given weight is felt. The two maps match with each other within the limits of experimental error (Gilmer). Thus it seems clear that the same receptors are involved in vibratory sensitivity as in simple pressure or touch sensitivity.

There is a similar story for prick pain and itch. With either a needle (see Rothman) or an electrical stimulus (Bishop), one can find the 'spots' that produce the experience of pain—a sharp pricking sensation. Then, by adjusting the needle or the electrical stimulus to give a few repeated stimuli, one can produce 'itching' sensations. The 'spots' that will give 'itch' are the same as those which will give 'prick pain.' Thus it is now rather well accepted that 'itch' is a variant of the pain experience and employs the same sensory mechanisms (Rothman).

The experience of 'tickle' is the last member of our list. And we are least sure about what it is. For one thing it is not feasible to map 'tickle' spots. The reason: tickle is something we experience when adjacent points on the skin are touched lightly in rapid succession. Thus to experience tickle you must have several points on the skin touched. That leaves the matter mainly to surmise. The common view of tickle is that it is a special variety of touch sensation, although some have supposed that it is really a variety of itch (Rothman), involving very weak 'pain' sensations. Whether 'tickle' is an 'itch,' a 'touch,' or a combination of the two (Bishop), no one believes that it is a primary sensation. We are therefore free to call it a derived experience.

Patterns of Experience. So far the picture seems simple. There are four basic varieties of cutaneous experience—and by implication four receptor mechanisms—and all other types of experience are made up of these four components. Such a statement, although perhaps true from a physiological point of view, is a bit misleading. We must continually bear in mind that sensory phenomena are not simple additions and subtractions of a few basic elements. In all the senses that we have surveyed, we have seen convincing evidence that any quality of experience is the outcome of a fairly complex pattern of sensory processes. And so it is in cutaneous experience too.

Here the pattern may be one of spacing and timing as well as of combining basic sensory components (Bishop). In everyday life, we seldom feel pain without touch, nor warmth or cold without touch, for the same stimulus that produces 'warmth' or 'cold' or pain also can be felt as 'touch.' Moreover, though itch may be tied up with our pain mechanisms, in a very real sense it is unique—it makes us scratch. The uniqueness is in the temporal pattern of events and in our reaction to it. Tickle is similarly unique because of the pattern of receptors involved and their order of stimulation. So, although we may break sensation down into four components—and there is more to follow on this point below—we must not miss the point that cutaneous experience is always the result of some particular pattern of sensory events.

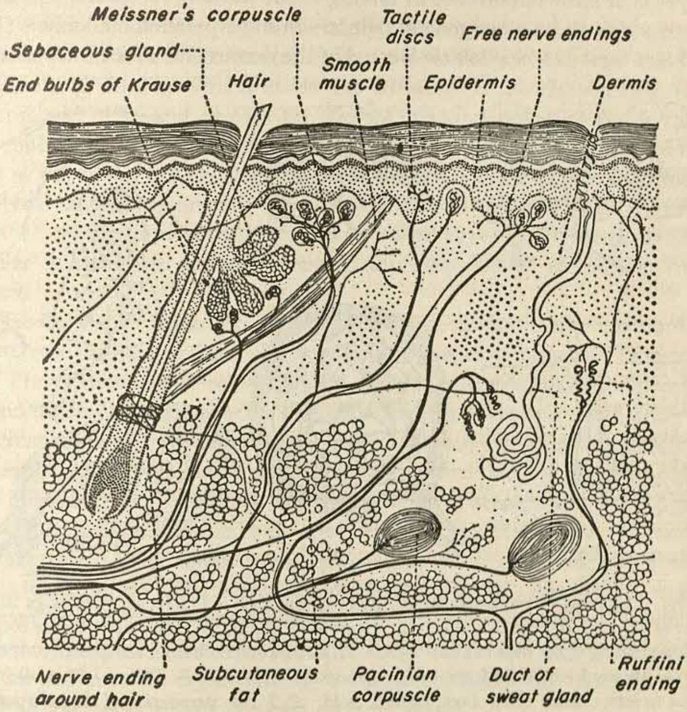

FIG. 95. Schematic drawing of a cross section of the human skin. Not all the structures in the diagram are to be found in any one area of the skin. Heavy lines are for myelinated fibers, and light ones stand for unmyelinated fibers. (*After Woolard et al. From E. Gardner. Fundamentals of neurology. Philadelphia: Saunders,* 1947. *P.* 111. *By permission of the publishers.*)

THE RECEPTORS FOR THE SKIN SENSES

By now you have been reminded several times of Müller's concept of specific nerve energies: our qualities of sensory experience rest upon differences in the receptors and nerve fibers responding to different kinds of stimuli. This concept has been a guiding idea in research in all the senses and just as much in the skin senses as in any other. In fact, no sooner had punctiform sensitivity for the different qualities been discovered (1884) than investigators set about looking for the receptors of the skin that give rise to the cutaneous qualities. This is the story of what they found.

General Structure of the Skin. In a cut down into the skin, such as you see in Fig. 95, there are three general zones of interest. The outermost zone is the *epidermis*. A second zone just below it is the *corium* or *dermis*. Finally, below that is subcutaneous *adipose tissue*, which strictly speaking is not part of the skin yet is of some importance in talking about the skin receptors.

Now, notice these other general points. In some parts of the body supplied with hairs there is a hair follicle located in the dermis and subcutaneous layers. This follicle is a narrow sort of chamber from which the hair grows out through the epidermis. It is supplied with sebaceous glands. Also found throughout the skin are sweat glands, embedded in the adipose tissue and supplied with ducts leading out through the epidermis to the surface. Of interest, finally, is the blood supply or vascular structure. One finds no blood vessels in the epidermis, but both the dermis and adipose layers are liberally supplied with small blood vessels. These, as we shall see, have played an important role in ideas about the skin receptors.

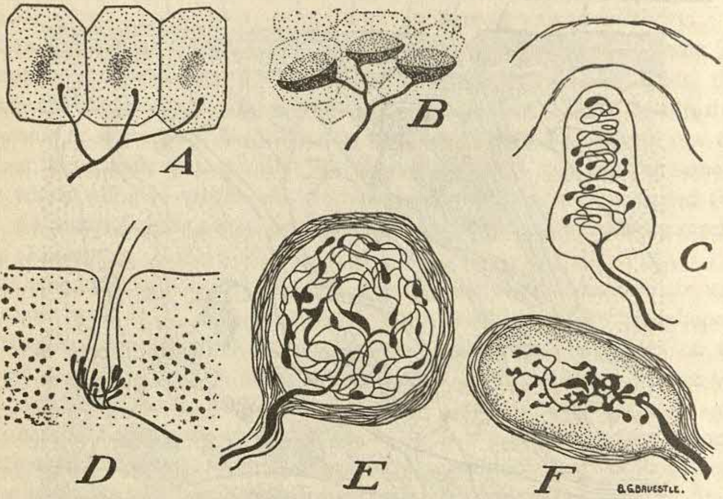

FIG. 96. Diagrams of the principal receptors of the skin. *A*, free nerve endings from the cornea of the eye; *B*, Merkel's cells from the snout of the pig; *C*, Meissner's tactile corpuscle; *D*, basket ending at the base of a hair follicle; *E*, Krause end bulb from the human conjunctiva; *F*, Golgi-Massoni corpuscle from the human skin. (*From J. F. Fulton. Physiology of the nervous system. 2d ed. New York: Oxford,* 1943. *P.* 3. *By permission of the publishers.*)

Encapsulated End Organs. In addition to these general aspects of skin structure, histologists long ago observed the presence of encapsulated end organs. Such end organs occur in the dermis and adipose layers. As their name implies, these are nerve endings surrounded in whole or in part by a capsule of tissue. You will find some examples in Fig. 96. These organs are rather easy to see under a microscope with the appropriate staining techniques.

It is no wonder, therefore, that investigators in their search for specific skin receptors have pounced on the encapsulated end organs as the answer to their problem. What they have done, in fact, is to classify the organs into several types and then endow each type with responsibility for a different quality of sensation.

The encapsulated end organs certainly vary a great deal in size, shape, and structure. This fact encourages attempts to classify them. So one type of corpuscle (*C* in Fig. 96) is called the Meissner corpuscle, another (*E*) the Krause end bulb, and another the Ruffini cylinder (not shown). A complete list contains many more names and supposed types of encapsulated end organs. But as the process of classification has gone on, it has become more and more doubtful that there are any clear-cut differences between these various end organs. Rather, it now seems that there is a great variety of them, all basically similar in structure and none having any clear line of distinction from all others.

Distribution of Corpuscles. Seventy years ago, investigators were more naive. They were inclined to think of a few simple types of end organs. One of them, von Frey, attempted to correlate each of the cutaneous qualities with one type of end organ (see Dallenbach). To find clues, he compared the distribution of different corpuscles in different regions of the body with differences in cutaneous sensitivity in these regions. It seemed to him that the Meissner corpuscle was more frequent in regions of the body where sensitivity to touch stimuli is greatest. The Krause end bulb appeared most plentiful where cold sensitivity was greatest. And another corpuscle, the Ruffini cylinder, seemed to correlate in its distribution with warmth sensitivity. Finally, free nerve endings—without any capsules—were correlated with pain sensitivity. Von Frey, therefore, proposed that the Meissner corpuscle is the organ of touch, the Krause end bulb the organ for cold, the Ruffini cylinder the organ for warmth, and the free nerve ending the pain receptor organ.

Local Studies. Giving support to this theory of the skin receptors were some studies in restricted regions of the skin. One was on the conjunctiva of the eye (Strughold and Karbe). This is sensitive to cold. Yet the only encapsulated end organs found there, aside from free nerve endings, are Krause end bulbs. In the experiment—a daring one—the eye was injected with methylene blue so that the Krause end bulbs were stained and therefore easily seen. The points that were sensitive to cold, in general, corresponded to Krause end bulbs. Important, however, were exceptions to the rule. Sometimes the cold spots and the Krause end bulbs did not correspond.

In another, more recent experiment the male prepuce was the region studied (Bazett *et al.*). Here there are about 15 cold spots per square centimeter and about 1 warm spot per square centimeter. The count for numbers of Krause end bulbs and Ruffini cylinders is just about the same as the number of spots. This correlation makes some people believe that von Frey was right in naming these encapsulated end organs as thermal receptors.

But it takes more than a very rough correlation between regions of sensitivity and regions of greatest numbers of end organs—which are very difficult to identify correctly anyway—to show that a given structure is *the* receptor for a particular sensory quality. The notion, however, is simple and attractive. It therefore appears in many textbooks, not only in general psychology but in advanced physiology as well. Yet it has never been more than a hypothesis, and the direct evidence for it is not very good, as we shall see.

Evidence from Biopsies. A much better experiment than any we have talked of so far is to find out what receptor in the skin underlies a sensitive spot. The straightforward way of doing this experiment—but somewhat disturbing to the subject—is to make maps of the skin for 'cold,' 'warmth,' or 'touch' spots, then cut out that portion of the skin, stain it, slice it, and look at it under a microscope to see what is there. The results of this kind of experiment ought to be rather decisive.

The experiment has been done, and many times. The verdict goes against the idea of encapsulated end organs and for a rather different conception of the skin receptors. From 1886 to the present the experiment has been done many dozens of times (see Gilmer). With hardly an exception, no one has found encapsulated end organs connected with any of the qualities of sensation. Of course, if you look for something and cannot find it, you cannot say whether you missed it or it was not there. When a lot of people with different biases and techniques look and cannot find it, the best guess is that it is not there. And so it seems in the case of encapsulated end organs.

Neurovascular Networks. What investigators almost invariably do find, using biopsies of tissues taken from sensitive spots, is free nerve endings and blood vessels. Often they find them combined and sometimes only free nerve endings. An example of such an ending in the epidermal cells is shown in Fig. 96. Free nerve endings, however, are by no means confined to the epidermis. They richly supply parts of the dermis and adipose tissue, particularly those parts with ramifying blood vessels. In any case, they consist of nerve twigs that fray into several fibrillae and end abruptly on the tissue cells without getting involved in any complex encapsulated organs.

The description of nerve endings and plexuses is the one point in common throughout the various experimental biopsies. Some investigators were examining tissue under cold spots, some that under pain spots, some touch, and some warmth (see Gilmer). Although they seldom found encapsulated end organs, they describe all sorts of nerve endings, some as simple as that illustrated in Fig. 96 and some with more complex ramifications and plexuses of nerve fibers. All this work with biopsies, then, points clearly in one direction. Free nerve endings, simple or complex but not encapsulated, can serve as the receptors in any or all of the cutaneous senses.

There is another point of importance which runs through most of the accounts of biopsies: the intimate relation between nerve endings and vascular networks of arterioles and venules. Most biopsies and, indeed, most descriptions of the nerve fibers of the skin indicate that nerve endings obviously are directly serving the vasculature. This particular relation of nerve fibrillae and blood vessels has given rise to some notions about receptor functions which we shall take up a little later.

The Glomus Body. Before we leave this point we should consider a special aspect of this neurovascular relationship. In a recent set of biopsies, a special type of neurovascular network called the *glomus body* has turned up in many of the specimens (Gilmer and Haythorn). It is an intricate structure in which arterioles anastomose with venules. It is fed by a set of arterial canals and empties into a venous network. The glomus body has been recognized by histologists only in recent years. Now that it is recognizable, it is being identified where pressure spots, and probably also where temperature spots, exist.

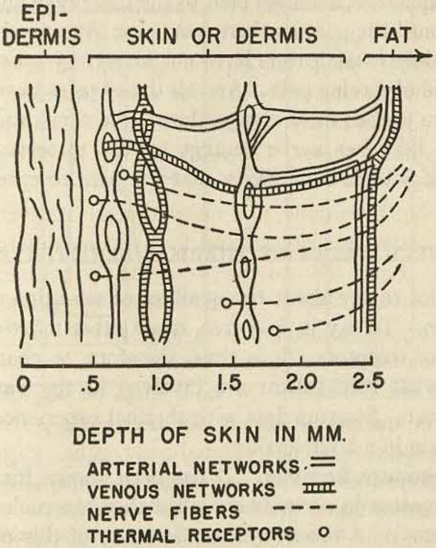

FIG. 97. Diagram of the neurovascular networks of the skin. There are no nerves or blood vessels in the epidermis. Just under it, however, are venous and arterial networks which connect up with the arteries and veins shown at the right in the fatty subcutaneous layer. Nerve fibers come in and end near the networks. Circles indicate the most likely positions of nerve endings of receptors. (*After Bazett,* 1943.)

But let us note that there is nothing unusual about this combination of nerve and blood vessel. All over the body, nerves and blood vessels are closely related, for the large nerves and vessels as well as the small. The relation can be seen, too, in the embryological development of organisms when their nerves and circulatory systems are being laid down. There are probably two good reasons for the relation, one mechanical and the other nutritional. As a mechanical matter, nerve fibers when they are growing out to their peripheral destinations tend to follow a channel of least resistance such as that afforded by a blood vessel (Weiss). Then, too, since nerves need plentiful supplies of fuel at the right time, they cannot get too far away from the blood stream and still survive. This is just another aspect of the fact that the nervous system has the best blood supply of any organ in the body (see Fig. 97).

Receptors for 'Pain.' Von Frey, the original proponent of specific receptors for the cutaneous qualities, ascribed pain to the free nerve endings. From the time of his work until the present there has never been much reason to doubt the notion. Certainly investigators have not found any other receptor organs that they suspected of serving pain. And all the biopsies in which tissue under pain spots has been excised have always shown free nerve endings as the main possibility. Now that free nerve endings appear to serve other cutaneous qualities as well, it is even more likely that the pain receptors are free nerve endings.

MECHANISMS OF THERMAL SENSITIVITY

There is still a lot to say about the qualities of sensation and the receptors that underlie them. To say it, however, raises other more specific questions about the action of receptors. It is time, therefore, to change our approach and to see just what mechanisms are involved in the various qualities of cutaneous experience. Starting first with thermal experience, we shall return to pressure and pain in a later section.

Nerve as Temperature Receptor. It has been known for a long time that potentials can be gotten in nerve fibers when they are cooled or warmed (see Granit and Skoglund). A recent systematic study of this effect throws some light on the problem of thermal receptors (Bernhard and Granit). The technique in the study was to place a small thermode—a sort of cuff whose temperature can be controlled precisely—around a bundle of nerve fibers and measure the resulting potentials. You can see the results in Fig. 98. They illustrate the two electrical changes that follow cooling or warming. One is a "local potential" difference between the normal and the cooled or warmed region of the nerve. The investigators call this potential the generator potential because they believe it is the fundamental potential that is responsible for other nervous effects. You can see in Fig. 98 that this potential may be several millivolts in strength and that it is larger or smaller, depending upon the degree to which the nerve has been warmed or cooled.

The second electrical change is something you might expect—a series of nervous impulses. As you see in Fig. 98, the frequency of these impulses increased and decreased according to the change in temperature produced in the region of the nerve stimulated. You will note, too, that cold (lowered temperature) is somewhat more effective in evoking both generator potentials and nervous impulses than is warm (increased temperature), but both are effective. The nerves in the study, incidentally, were mixed sensory nerves, not those carrying just thermal messages. And the upshot of the matter is that a temperature differential or gradient in a nerve is capable of exciting both local and propagated nervous effects.

Gradients of the Skin. Fortunately, it is possible to tie up this fact with some knowledge about the thermal receptors of the skin and the gradients of temperature involved in their excitation. A few years ago Bazett and his collaborators carried out an ingenious set of experiments on this point. They actually measured the gradients of temperature in the skin of the forearm as you see it sketched in Fig. 99. They did it by thrusting a very small thermocouple into the skin to various depths.

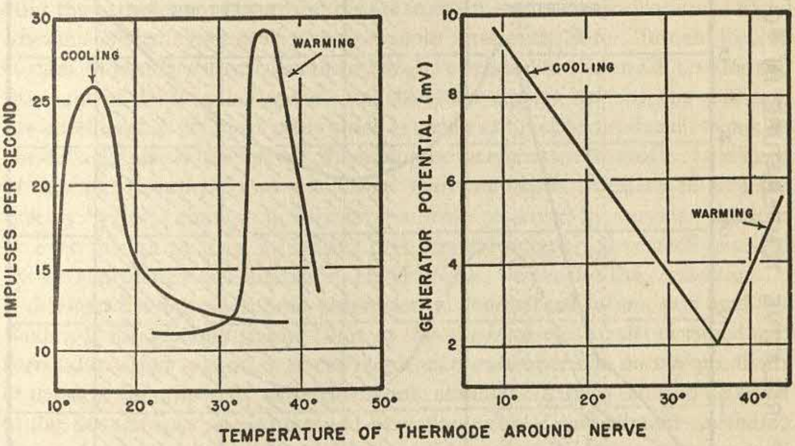

FIG. 98. Some results of experiments on nerve as a model of a temperature end organ. On the right is the generator potential—local steady potential—as a function of slow cooling or warming of the nerve. On the left is the number of impulses per second for different temperatures. One curve is for slow warming of the nerve; the other is for slow cooling of it. These results are simply examples of what is seen in experiments with warming and cooling nerves. (*After Bernhard and Granit*, 1946.)

You can see that the temperature of the skin rises rather sharply between the outer surface of the epidermis and the first layers of the dermis. The temperature drops slightly in the middle and lower layers of the dermis, only to rise again in the subcutaneous adipose layer. By looking at Fig. 98 you can see why these gradients occur—it is because of the distribution of small arteries and veins. A small network of arteries in the outer dermal region causes the first gradient of temperature and its peak. The 'hollow' in temperature in the lower dermis corresponds to venous networks, which have somewhat cooler blood being returned from the periphery toward the heart. The higher peak of temperature in the adipose layer goes along with the presence of the larger arteries and veins distributing blood to and collecting it from the periphery.

Location of the Thermal Receptors. Bazett and his colleagues have supplied some other important aspects of the story. They have determined approximately where the warmth and cold receptors are located with respect to these thermal gradients in the skin. To do that they used the male prepuce or foreskin, placing a thermocouple on one side of it and a thermal stimulator on the other. With this combination of instruments they were able to correlate changes in temperature of the skin with the time and temperatures at which subjects reported thermal experience. The net result of their experiments was to tell us that the 'cold' receptors lie near the surface of the skin, usually less than 1 mm. in depth, whereas the 'warmth' receptors are somewhat deeper, about 1 to 3 mm. below the surface. The relative locations of these receptors are sketched diagrammatically in Fig. 99.

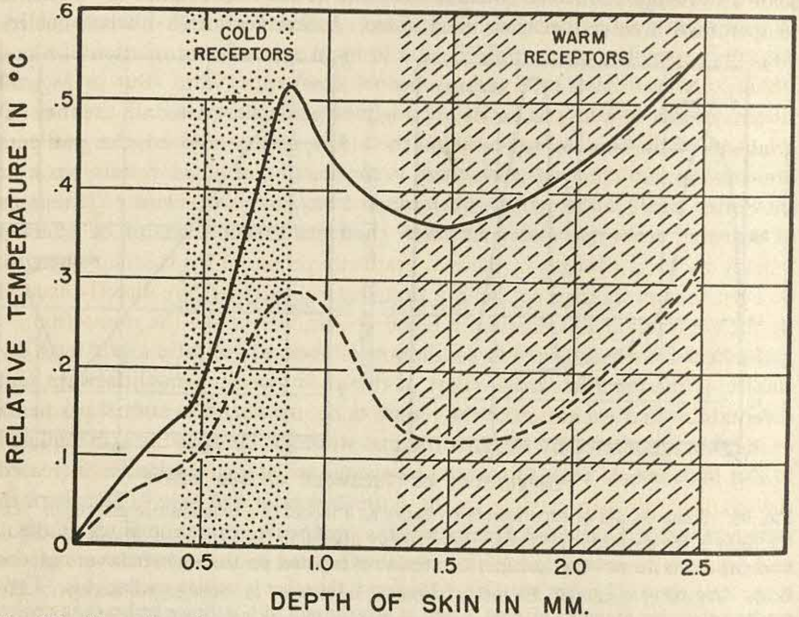

FIG. 99. Thermal gradients of the skin. The solid line is for measurements taken when the skin was flushed with blood, and the broken line is for normal skin. The temperatures are the differences between the temperature of the surface of the skin and that at various depths. The probable positions of the cold receptors and warm receptors are indicated. Notice how they are related to thermal gradients. Note, too, how the gradients are related to the vascular networks depicted in Fig. 98. (*After Bazett*, 1943.)

Theories of Excitation. With this information in hand, it is rather easy to see how receptors are excited by thermal stimuli. Actually, during the last 15 or 20 years there have been three more or less opposing theories of thermal excitation. There is no need to go into them in detail nor to consider all the arguments pro and con. It is helpful, however, to see what they are, for each of them has its merit.

Vascular Theory. First of all is Nafe's so-called *vascular theory.* Impressed by some of the connections between thermal experience and changes in blood vessels—such as the 'chills' in fever—Nafe has come to believe that the temperature receptors are in the walls of the blood vessels. For him, the experience of cold comes about because blood vessels contract somewhat when cooled. And the experience of 'warmth' results from an expansion or dilation of blood vessels. Nowadays not very many people agree with Nafe. But in Fig. 99 it is easy to see how a vascular theory might be plausible. After all, the thermal gradients of the skin do depend upon the blood supply. Indeed, the gradients are considerably changed when there is constricting of blood vessels—look at the dotted curve in the figure. Then too, the receptors are all located in regions of vascular networks, and you would therefore expect them to be affected quickly by local changes in thermal gradients produced by vascular changes. So even though we may not believe that thermal receptors are directly excited by the contraction and dilation of blood vessels, we can see the connection.

Gradient Theory. A second conception of thermal excitation, put forth by Bazett, is the *gradient theory.* Part of this theory seems straightforward and acceptable—that excitation of the receptors occurs when the normal gradients of the skin are altered by external thermal stimuli. Thus, in the skin depicted in Fig. 99, the cold receptors would be excited when a cold stimulus increased the gradient already existing in the outer layers of the skin. The warmth receptors would be excited when a warm stimulus overcame the outer gradient and produced a reverse gradient extending inward to the deeper layers of the skin. Another part of Bazett's theory, however, is harder to accept. He believes the Krause end bulbs to be the receptors for cold and the Ruffini cylinders the receptors for warmth. We have reviewed some of the evidence from biopsies against this notion. Still other negative evidence will be discussed in a moment.

Concentration Theory. Finally to be mentioned is Jenkins's so-called *concentration theory* of thermal excitation. He believes that the thermal receptors are free nerve endings, not encapsulated end organs such as the Krause end bulb or the Ruffini cylinder. For this position he has not only the biopsy evidence but also the results of many mapping experiments which he himself has carried out. An example of such mappings is shown in Fig. 100. There you see, not a few spots sensitive to thermal stimuli, but some areas that are very sensitive and others that are not so sensitive. It is as though rather numerous nerve endings varied in their concentration, sometimes being densely packed and sometimes being sparser—thus the name, *concentration theory.*

On this point Jenkins seems to be right. In addition, however, to explain thermal adaptation and some other phenomena of temperature sensitivity, Jenkins has postulated some intervening chemical reactions—thermochemical events—set off by thermal stimuli but the immediate cause of nervous impulses in the thermal receptors. He may or may not be right on this point. Our recent knowledge of the slow "generator" potentials may make it unnecessary to assume thermochemistry in the excitation of thermal receptors.

What now seems to be the best synthesis of these three theoretical positions goes like this: from Jenkins we take free nerve endings as the receptors, from Bazett the idea of thermal gradients, and from Nafe the notion of a close connection between the blood vessels and the thermal receptors. The first thing to happen, then, when a thermal stimulus is applied is a change in the thermal gradient of the skin—which may be affected by the blood supply at that moment. The change, in turn, subjects free nerve endings to a temperature gradient, which induces in them a slow local "generator" potential. This, finally, produces impulses in the nerve fibers which travel on their way to the nervous system. At all stages of the process the conditions of blood flow, controlled by the vasculature, can make a considerable difference.

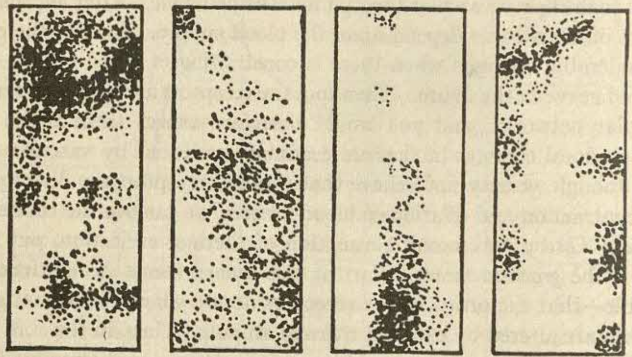

FIG. 100. Maps of the concentrations of thermal receptors on four different regions of the skin as deduced from tests of cold sensitivity. (*After W. L. Jenkins. Studies in thermal sensitivity:* 12. *Part-whole relations in seriatim cold-mapping, p.* 383. *J. exp. Psychol.*, 1939, 25, 373–388. *By permission of the American Psychological Association.*)

Phenomena of Thermal Experience. This picture of the events in excitation of the thermal receptors explains a number of phenomena observed in various experiments with thermal stimuli. To save time, let us run over them very rapidly (see Woodworth).

1. Reaction time to warm stimuli should be longer than to cold stimuli, because the warm receptors are the more deeply situated. It is.

2. The threshold for 'cold' should be less than that to 'warm,' because the cold stimulus merely exaggerates the existing gradient, whereas a warm stimulus must overcome the external gradient and produce a reversed gradient deeper in the skin. Such is the case. The cold threshold is, typically, somewhat smaller than that for warm, although the exact values vary with different conditions and regions of the body.

3. There ought to be 'paradoxical' cold, *i.e.*, stimulation of the cold receptors occasionally by warm stimuli, for warm, in overcoming the epidermal gradient, might reverse it enough to stimulate the fiber. Such an effect has been known for a long time. So also is paradoxical 'warmth,' but this phenomenon is rare, as one might expect, for it should be very difficult for a cold stimulus to overcome the heating effect of the peripheral blood supply (see the first peak in Fig. 99) and change the gradient in the region where the warm receptors are located.

4. One might expect adaptation to warm to be more rapid than that to cold, for the warmth receptors are protected by the "internal heating elements" of the skin's blood vessels. This expectation has also proved true in experimental fact.

5. Because the 'warm' receptors are more deeply situated and affected more directly by vascular temperature changes, one might expect maps of the 'warm' spots to be somewhat less stable than those for 'cold.' That, too, is true.

6. Finally, one might expect anything affecting blood supply to affect temperature sensitivity. For example, when one hand is exposed to a change in temperature, the threshold of sensitivity in the other hand also changes (Woollard *et al.*). Because we know that the blood vessels in the other hand are constricted or dilated by thermal stimuli in one hand, this phenomenon has been used to argue for a vascular theory of thermal experience. Actually, the phenomenon is predictable from changes in thermal gradients of the skin produced by vascular changes (see Fig. 99).

This list of phenomena of thermal experience could be expanded to great length. In each case it would be easy to explain the phenomenon in terms of the mechanism that our present knowledge depicts for us. This short list of examples, however, should be enough to show that our understanding of the peripheral mechanisms underlying thermal experience is now reasonably good.

SENSORY MECHANISMS FOR PRESSURE AND PAIN

Pressure and pain are separate qualities of experience. You have already heard some of the reasons for believing that. In experiments, however, it is hard to separate them. When you stick a man with a needle you are also touching him, and he feels both pressure and pain. Only by some rather ingenious methods in animals and man is it possible to separate the sensory mechanisms of the two experiences. So we find it easier to start out talking about them together, and later in the section we can make the appropriate distinctions between them.

The End Organs. Histologists have done a good job of telling us about the receptors for pain and pressure. They have sliced up sections of skin from various parts of the body, stained the slices, and described carefully what they saw. Their descriptions include several points of interest for understanding what goes on when the experiences of pain and pressure are aroused (Woollard *et al.*, Tower).

For one thing, they report a good deal of ramification and interlocking of nerve terminals. Small groups of fibers leave the main nerve trunk in the subcutaneous adipose layer. In the dermis these small fiber groups split up into individual nerve fibers. Then in the upper dermis and epidermis, each fiber divides into a number of branches. These branches, however, come back together again and split off again from one another, making a plexus, or anastomosis. Out of the plexus arise the numerous small terminals serving the skin receptors.

There are two important points to keep in mind about the small nerve plexus serving the skin (see Tower). One point is this: the branches of two different fibers (of different neurons) do not join together. Each neuron preserves its identity in the terminals. The interlocking in the plexus is only of the branches of one fiber. The second point concerns the area served by one fiber: this can be much larger than one might expect. Sometimes, as in the viscera of the frog, one fiber or neuron unit may serve as much as 6 sq. cm. There are some regions of the skin of the frog and of man where the area is more than 1 sq. cm. In more sensitive regions, however, the area is smaller. On the back of a man's hand, for example, the net or plexus of one fiber serves about ⅓ sq. cm., and on the monkey's thumb the area is about 1 mm.

Another point of interest in the histologists' studies is the overlapping of innervation. Although the branches of different fibers do not join with each other, they serve overlapping areas of the skin. Thus a needle or a hair touched to any part of the skin is likely to stimulate the branches of more than one fiber. The degree of overlapping of terminals varies greatly from one region of the body to another. It looks, too, as though the overlapping is greater for pain receptors than for pressure receptors. Even in the case of complex encapsulated end organs such as the Meissner corpuscle or in the case of hair follicles (known to be organs of pressure), a single end organ may be innervated by the branches of several different neurons. So in thinking about either free nerve endings or more complex end organs, we must realize that the stimulation of any spot on the skin usually affects the terminals of several different fibers.

The Peripheral Unit for Pain. We do not have to trust entirely to the histologists' reports for this conception of the receptors. A very neat method has been devised for mapping the sensory units for pain in man (Bishop). The main trick of the method is to use a short electric spark for the stimulus. A voltage of the right amount applied to an electrode near the skin, but not touching it, will cause a spark discharge to the skin. Either a pressure or a prick-pain experience will result—sometimes both. Points that give only the prick-pain experience can be selected and marked, and with appropriate adjustments in the voltage, the thresholds of the points can be found.

This method gives the conventional map of "pain spots" that can be gotten with needles or direct electrical stimuli. But it also does more than that. By using spark discharges of the right strength, it is possible to stimulate directly through the skin the nerve fiber whose branches serve the areas that have been mapped. Once several fibers have been located in this fashion, it is possible to anesthetize the fibers, singly or in combination, by squirting a little cocaine into the skin along the route of the nerve fiber. With various fibers anesthetized, one can remap the points sensitive to prick pain and see just what areas of the skin are served by various neuron units.

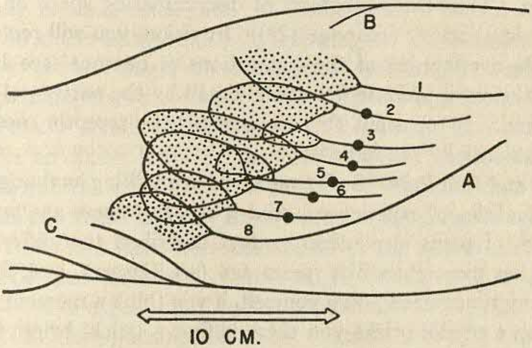

FIG. 101. Sketch of pain units mapped in Bishop's experiment. The dotted areas are the endings of the nerve fibers 1, 2, etc., which are branches of the *A* group of nerve fibers. *B* and *C* are other groups. The black dots show the spots that were anesthetized. By blocking nerve twigs in different combinations and mapping the area of remaining sensibility for pain, the maps were constructed. (*Redrawn after Bishop*, 1944.)

The results of one such experiment are pictured in Fig. 101. There you can see the areas of overlap of eight different sensory units. These areas were found by anesthetizing the fibers serving them at the points indicated with large black dots. For example, by anesthetizing at points 2 and 3 and at points 7 and 8 and remapping the skin, the areas serving unit 4 could be mapped, and so on with the other units. In this way the peripheral units for pain on the forearm can be directly measured. You can see that they are relatively large—of the order of several centimeters—and the degree of overlapping is great.

Localization. Before we go on to anything else, it is important to see clearly the meaning of this overlapping of sensory units. Consider first the punctate sensitivity of the skin. We can be quite sure now that the "spots" on the skin for different qualities of experience do not represent separate receptors. Instead, they are simply the points of greatest sensitivity in a much larger net of an individual fiber. This is a fact proved in the experiments with the electric-spark stimulus for prick pain. It was in the center of the area of a sensory unit that there was the greatest sensitivity (Bishop). In the margins of the area which overlap with other areas, thresholds were the poorest (Bishop).

So Jenkins's concentration theory of punctate sensitivity is essentially correct. The "spots" are just the central, most sensitive parts of the area of a sensory unit—the ramifications of one neuron's fiber.

There is a second important point to be noted from these experiments on the overlapping of sensory units. We know what spot on our skins is being stimulated by the *pattern* of receptors that are excited (Tower). A stimulus, unless it is very small and placed in the center of one sensory unit's distribution, ordinarily excites more than one unit. It is the difference in stimulation of units serving a region that gives us the local sign, *i.e.*, lets us localize the place of stimulation. Thus the mechanism of discriminating space on our skins is like that for visual acuity (see page 128). In vision, you will remember, there is considerable overlapping of the connections of neurons (see Fig. 48), but we can nevertheless appreciate fine visual detail by the pattern of visual fibers that are excited. It turns out that the somesthetic receptor mechanisms are organized in essentially the same way.

Prick Pain and Dull Pain. So far we have been talking as though pain is one of the four qualities of experience. And it is. But there are two kinds, not just one kind, of pain. Investigators first described two different kinds of pain experiences more than fifty years ago (see Gasser), and they have described it many times since. You yourself, if you think a moment, will remember that when a needle pricks you there is first a quick, bright flash of pain that you might call a *prick* and then a duller, longer lasting pain. Of course, if we had to rely entirely on subjective reports, we might not be sure that there are really two distinct pains. Physiological experiments, however, tell us that there are (Gasser).

There are two kinds of nerve fibers serving the sensory units of the skin. We call them the *A* and the *C* fibers. *A* fibers are relatively large and are medullated. They give large impulses and conduct quite rapidly. The *C* fibers are very small, they are unmyelinated, and they have very small impulses, which travel quite slowly. The *A* fibers, the fast-conducting fibers, are the ones that give the quick, bright prick pain. The *C* fibers carry impulses for the slow, longer lasting dull pain. And this is how we know:

Asphyxia and cocaine are two methods of anesthetizing sensory nerves. They act, however, somewhat differently on the *A* and the *C* fibers. Cocaine blocks the *C* fibers first. Only later, after the drug has had more time to penetrate fibers, does it make the *A* fibers insensitive. Asphyxia, on the other hand—which, if you have forgotten, is the term for depriving cells of oxygen—hits the *A* fibers first. Only when asphyxia has become very severe do the *C* fibers also become anesthetized.

It is relatively simple to compare these facts about anesthetizing the *A* and *C* fibers with the way in which pain disappears during asphyxia, and several investigators have done it (see Gasser). The arm can be asphyxiated simply by placing a pressure cuff around it, which cuts off the blood supply. As the asphyxia progresses, a person first loses the sense of touch, then temperature, and the last to go is pain. This pain, however, is reported as slow or dull pain. The reaction time to it is longer than to a needle prick in the normal arm—in fact, it is the time you would predict, knowing the velocity of conduction in the slow, unmyelinated *C* fibers. Sometime during the progress of asphyxia, the prick pain drops out, leaving only the slow dull pain.

The opposite happens when cocaine is injected into the region of a nerve to produce local anesthesia. Dull pain disappears first. Then temperature sensitivity drops out. About the last experience a person feels before he becomes entirely numb is prick pain. A needle prick is felt for a brief instant, but there is no longer lasting dull pain following it. The reaction time for such experiences, in the last stages of cocaine anesthesia, is what would be expected if the prick-pain impulses are carried in the relatively fast fibers of the *A* group.

There are many details of this story that we do not have time to go into. They all leave no doubt, however, that there are two sensory mechanisms for pain, one fast and the other slow, one bright and the other dull.

Fiber Types and Other Sensory Experiences. Several years ago, when fibers of different types and sizes were discovered in the nerves serving the skin, there was hope that each type of fiber might be responsible for one of the different qualities of experience. Such a hope is now fading fast. Investigators have studied the disappearance of touch, warmth, and cold experiences with cocaine and asphyxia as anesthetics. Except for the difference between prick pain and dull pain, no other clear-cut distinctions can be made. Certainly impulses for touch and temperature are carried in the *A* fibers along with those for prick pain. Within the *A* group, too, it looks as though the impulses for touch are somewhat larger and travel faster than those for temperature, but there certainly is a good deal of overlap. Investigators have not been able to decide, however, whether impulses for thermal experience are also present in the *C* fibers. If that is the case, we should have to speak of bright and dull cold and bright and dull warmth as well as of bright and dull pain. We just do not know about that problem at present.

Pain from Excessive Stimulation? Now we ought to consider briefly some other questions about pain and what produces it. One question is of long standing, and there has been much controversy about it: Can the experience of pain be aroused by the excessive stimulation of receptors that also give the experiences of touch or warmth or cold? One group of investigators (Nafe) has always said, "Yes." This group, in fact, has argued against specific receptors for each of the qualities of experience. They have believed that the qualities of experience are interpretations of patterns of impulses coming from the skin receptors. In particular, they have considered pain to be the result of excessive stimulation of any of the skin receptors.

As matters stand at present, there is no clear disproof of such a view. There is, however, proof that pain is not always the result of excessive stimulation.

Moreover, all the facts of modern research stack the odds against the view. Here are just a few of the facts that argue for pain as a separate modality, one that is not just the result of excessive stimulation.

Consider the sensory endings associated with the hairs of the skin. They are quite sensitive to pressure. They can be stimulated quite intensely with a rod vibrating at high frequencies. Such stimulation, however, never gives rise to the experience of pain (Adrian).

There is another similar experiment with the frog in which electrodes placed on the sensory nerves from the skin provide a record of impulses in the nerve (Cattell and Hoagland). The skin of the frog was stimulated intensely with an interrupted air jet. In the nerve, this produced impulses as frequently as 300 per second—a value that is just about the maximum rate possible in the nerve's fibers—but there was no pain. At least, the frog's behavior showed no evidence of pain.

There are other indirect arguments, but these should suffice. The excessive stimulation of the receptors for pressure does not, so far as we know, give rise to pain. That fact, taken together with what we have already learned about maps of "pain" spots and spots for other experiences, makes us believe that pain has its own receptors.

But there is another interesting question. What are the stimuli for exciting the pain receptors? We can feel pain, not only when we are stuck or cut but when it is too hot or too cold. That would suggest that any kind of intense stimulus, whether pressure or temperature, may excite pain receptors. Generally speaking, this seems to be true. Yet there are exceptions. The conjunctivum of the eye, is normally sensitive only to touch and to pain (except for the peripheral areas, which are also sensitive to cold). If one applies heat to the central cornea by radiant methods, an observer feels no pain (Nafe and Wagoner). Yet heat of the same intensity applied to some area of the skin is painful. In the cornea, then, excessive stimulation by heat does not produce pain. So, although strong stimuli, whether mechanical or thermal, seem often to excite pain receptors, they do not always do so. Is it possible that some pain receptors respond to all types of stimuli, while others can be excited only by one type of stimulus (Tower)? We do not know.

Receptors for Pressure. You are probably convinced by now that there are different receptors for the qualities of cutaneous experience. You have seen, too, that free nerve endings can serve in all the experiences. Thus a nice idea—that each experience comes about by excitation of receptor organs of different appearance—is exploded. You cannot tell by looking at the skin receptors what job they are doing in experience. Nerve endings can serve for pressure, pain, warmth, and cold.

There is, however, another point that should not be missed. The experience of touch or pressure sometimes comes from end organs that are more complex than free nerve endings. There is no doubt that, *e.g.*, the hair bulbs of the skin are usually organs of pressure sensitivity (Strughold). The odds are, too, that Meissner corpuscles also are touch receptors—although they certainly are not the only touch receptors. We have only correlations to go on, *viz.*, the fact that Meissner corpuscles, in hairless regions of the body, are more numerous where the sensitivity of the skin is best. But it is a fair guess that they are also pressure receptors.

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CHAPTER XII

SOMESTHETIC MECHANISMS

In the last chapter we were dealing with the skin and its sensory mechanisms. In this one we shall get beneath the skin. We shall consider first some of the sensory mechanisms of the interior of the body and then go, in the later part of the chapter, to the nervous centers and pathways that figure in the skin and proprioceptive senses.

ACHES AND PAINS

We have already had a good deal to say about the pain we feel from our skins, but there is much more to the story. There are a lot of pains and aches besides those of the skin—headaches, muscle aches, backaches, neuritis, neuralgia, and so on. These have always been of great interest to the physician and neurologist, who use them clinically to diagnose our ills. They also have always presented a number of phenomena that have been baffling and misleading. Today we do not fully understand the mechanisms of these deep aches and pains, but we know a lot more than we did several years ago (see Wolff and Wolf).

Deep Pain Receptors. In the last chapter we saw that there are two kinds of pain—bright and dull, or alternatively, superficial and deep—which are carried by two different sets of fibers. As far as we can make out, the bright-pain receptors are mainly located in our skins. The pains we feel beneath our skin are dull, or deep, pains. This kind of pain is much more poorly localized than bright pain. It also is conducted more slowly and over the small, unmyelinated or lightly myelinated fibers. It is the kind of pain we shall talk about now.

The receptors, just as in the case of the skin, are free nerve endings. They are found in all sorts of deep tissues of the body—blood vessels, mesenteries, linings of various organs, and muscles. The place, however, where the deep-pain endings are most often found is in the walls of blood vessels of various sorts, both large and small. This fact, as we shall see, is rather important in many of the phenomena of deep pain. There are many pain endings in the muscles of the body, but they probably do not serve the muscles directly. Instead, they go to the blood vessels which so richly serve muscle. This also is important in understanding pain.

The Spread of Pain. One of the most important features of deep pain is that it spreads, and it spreads in several ways (see Wolff and Hardy). The simplest and most direct way is a spread to a larger area than that which is the true site of pain. To take a simple example, if you hold one of your fingers in freezing water for a few minutes, not only does the immersed finger give you pain but you can also feel pain on the borders of the other fingers next to it. You feel pain bordering on the region that is getting the painful stimulus. That is the simple spread of pain.

More complicated and more baffling is *referred pain.* In this case, some other organ or tissue than the one being stimulated also seems to be painful. A person suffering kidney disease, for example, may have pains in his back. Or an infected tooth may give you not only a toothache but a headache as well. There are many such examples of referred pain, and they are a continual problem to physicians, who try to tell what is wrong with people by finding out where they are having aches and pains.

Mechanisms of Referred Pain. There have been some nice experiments in the last few years that tell us something about how and why we have referred pain. The simple spread of pain is the primary factor. This spread is often greater and involves more tissues than at first we might suspect. Spread of pain from one finger to the finger near by is relatively straightforward. The 'spread,' however, may sometimes go farther than that. In fact, we sometimes feel pain on the opposite side of the body from the part stimulated. To the neurologist, that is not so mysterious. He knows that the nervous system is 'hooked up' in segments so that certain areas of the body are served by each of the segments of the spinal cord. After pain impulses get into the spinal cord, moreover, there is ample opportunity for impulses to spread to the parts of the cord that serve other areas of the segment on both the same and opposite sides. There is, however, a simple rule for this kind of spread of pain: the spread occurs within the area of a spinal segment. If you know what areas are served by different segments, you can tell where to expect the spread of pain.

There is also a second mechanism of referred pain. This involves some reflex reactions to the primary source of pain. The most common and important reflex reaction is a spasm of the blood vessels in muscles in the general region of the pain. Such a spasm, in turn, causes more pain, because it cuts off blood supply to the tissue, creating an anoxia that is itself a painful stimulus to the pain fibers in the blood vessels.

Let us take just one simple example. Suppose you have a pain in your stomach due, say, to indigestion and stomach acidity. The pain impulses from the stomach go into the spinal cord. There they cause a reflex spasm of the blood vessels in your abdominal muscles. The local anoxia caused by this spasm stimulates the pain receptors in these blood vessels. The result is that you feel a pain in your abdominal muscles as well as in your stomach. That is a simple example of this second mechanism of referred pain. It accounts for many of the aches and pains which we think we have but which are not really there when the physician looks for them.

Hyperalgesia. There is just one other aspect of this story that deserves mention here. Sometimes we do not have a referred pain in a remote area but only a hyperalgesia, *i.e.*, some tissues remote from the true source of pain may be irritable and tender, they may be more sensitive to painful stimulation than usual. Such hyperalgesia, which may or may not accompany referred pain, is the same sort of phenomenon as referred pain. It is due to the spread of pain or to the secondary reflex effects that we just described.

It would take too much time to go into all the research that lies behind the statements we have just made. In general, the methods that have been used are (1) the anesthetization of primary and secondary areas of pain or (2) the sectioning of nerves from either or both areas. Whichever method is used, it will abolish the pain if the primary source of the pain is attacked, but it will do little good if applied only to the area of referred pain. It will reduce the hyperalgesia of a referred-pain area but not the pain itself. Thus, if we have a headache that is caused by a toothache, it will do little good to take a pill for the headache—it will not go away. A pill that cures the toothache, however, will also get rid of the headache. That is the practical point. The more general point of these experiments is that spread of pain involved in these effects is something that occurs in the central nervous system, not outside it.

The Causes of Deep Pain. A little later we shall come back to the central pathways for pain, but while we are considering the receptors and peripheral phenomena of pain, there is another question to ask: What is it that makes us have aches and pains? This is an important question and unfortunately there are several answers to it. There apparently are several different causes of deep pain in the body, and in some cases there must be a particular combination of conditions for us to feel pain.

Consider first the gastrointestinal tract. All of us know that we feel pain in it. Some of the sharpest and most severe of our pains seem to be in our stomach and intestines. Yet, in the course of surgery when people are conscious, attempts to induce pain by deliberately stimulating the stomach or intestines usually do not succeed. Indeed, a surgeon may scratch, pinch, or even cut many of the deep tissues of the body—the mesenteries of the intestine, the gut of the stomach or intestine, the parenchyma of the lung and liver—without provoking any pain at all. These conflicting facts have posed a mystery that has been hard to solve and has led to controversy.

Vascular Reactions. One of the keys to the mystery is the reaction of blood vessels. In the first place, these are frequently the site of pain stimulation. In muscles, for example, the pain endings probably do not serve the muscle fibers directly, and in any event, they are most numerous in the blood vessels serving the muscle (Kellgren). Experimental pinching and cutting may not directly stimulate pain endings in the blood vessels. In the second place, the engorgement of blood vessels accompanying the inflammation of tissue may be necessary in some way for pain stimuli to be effective. In one study, for example, the cutting of gut that was already greatly inflamed did arouse pain, even though that was not the case in normal gut. It is now safe to say that many tissues that are insensitive to experimental stimulation under normal circumstances become sensitive when there are vascular changes and inflammation—the kind of situation in which we usually feel pain. We cannot be sure just why this is true, but it seems to be.

Chemical Stimuli. Perhaps the explanation is chemical. Where there is excessive vascular engorgement or tissue inflammation there are usually toxins or irritating chemical conditions. At any rate, chemical factors are certainly of some importance in causing deep pain. In fact, recent evidence makes it look as though the pain we feel when there is prolonged muscle contraction or anoxia in muscle is really due to an excess of potassium produced by the anoxic or contracted condition. Certainly, too, it is easy to provoke pain by injecting chemical irritants into muscles and tissues. And because pain is sometimes not felt when pain fibers are cut but is felt when their endings are stimulated, some believe that there must be an intermediate chemical process which sets up pulses in pain fibers. According to this notion, free nerve endings liberate some substance when they are stimulated, and it is this substance that sets up the pain impulses. As you can see, it is hard right now to make sense of all we know about chemical stimuli in pain, but there can be no doubt that chemical factors are involved, at least some of the time, in producing pain.

The Causes of Headache. Perhaps it would help tie things together if we took one type of pain—the common headache—and told what we know about it. Headache has probably been studied from more different points of view and more thoroughly than any other type of deep pain. As matters stand today, we can distinguish six different types of headache (Wolff and Wolf), according to the factors that give rise to them: (1) pressure or pull on the veins leading to the venous sinuses of the brain, (2) pressure or pull on the arteries supplying the meningeal coverings of the brain, (3) pressure or pull on the arteries of the brain that make up its main blood supply, (4) distention and dilation of arteries within the brain and skull, (5) inflammation of any of the structures, such as eyes, neck muscles, skin, and so on, of the head, and (6) direct pressure by tumors on the sensory nerves of the head that contain pain fibers.

The last of this list, the direct pressure on sensory nerves, is fairly obvious. That is what you would expect. The fifth item, inflammation of associated structures, you may recognize immediately as referred pain. 'Eyestrain,' for example, may cause prolonged contraction of the neck and head muscles, and this may give rise to referred pain. Or pain from the eyes or neck muscles, by simple spread in the nervous system, may arouse pain impulses in the pathways from inside the brain and skull.

The first items that we listed above all have something to do with pressure or distention of blood vessels. That is probably the most important point to keep in mind. There are many direct causes of this kind of headache—brain tumors, 'hangover,' fever toxins, migraine, hypertension, sinus trouble, and other disorders—but all of them cause their pain through changes in blood vessels. More specifically, the cause of pain is a relaxing or distending of the blood vessels. Whether chemical factors expand them or high blood pressure distends them or some other sort of pressure in the brain pulls on them, the primary source of the pain seems to be a 'pinching' of the free nerve endings in the walls of the blood vessels by dilating them too much.

We have not given detailed experiments for all these statements. There are many experiments behind them, but to save time and space, we have simply hit the high lights of their results. There are many experiments, too, on pain in many other parts of the body. They all fall in fairly well with this general picture we have given you.

FEELING AND ANXIETY

The subject of feeling, *i.e.*, pleasantness and unpleasantness, is treated in most textbooks along with that of emotion. That is one way of doing it. From a physiological point of view, however, the problem of feeling is more closely related to the somesthetic mechanisms, both peripheral and central, than to those of emotional expression. That point may not be obvious, but you will see evidence for it as we go along.

The James-Lange Theory. For many years the most prominent physiological theory of emotion was that put forth by James and Lange, and the theory still has an important place in psychology today. The theory, however, was probably misnamed—it might better be called a theory of feeling than one of emotion—for the distinctive part of the theory concerns feeling.

In brief, the James-Lange theory goes this way: Some stimulus or event that we call an emotional situation comes along in the world. The first thing that happens physiologically is a reaction of our muscles and glands. This reaction, in turn, sets up impulses that go back into the nervous system, make their way to the cortex, and bring about an overt emotional reaction, as well as 'conscious experience' of emotion. The crucial point in the theory—the point that distinguishes the theory—is that our emotional experience comes from the somesthetic input from the muscles, glands, and tissues deep within the body.

As we shall see later, we now know that somesthetic stimulation is not necessary for the expression of emotional behavior, but that is beside the point here. The essential point of the James-Lange theory is correct in that there is an internal sensory basis for feeling. As we have seen above, tense contraction of muscles can cause anoxia and pain, or if not pain, at least discomfort. Autonomic responses of the blood vessels and the circulatory system can cause pressure and dilation of blood vessels, which cause discomfort or even severe aches and pains. That much we know. The remaining question is whether there is any more specific mechanism for feelings, both of unpleasantness and pleasantness.

Somesthesis and Feeling. Although pain may be prominent in feeling—we certainly feel 'unpleasant' when we suffer pain—it is not the only sensory aspect of feeling. We all know that touch, warmth, cold, and tickle also have something to do with whether we feel 'pleasant' or 'unpleasant.' If you ask people, they will usually say that warmth and tickle are pleasant—they feel 'good'—and that cold and pressure, at least extreme pressure, are unpleasant. That brings all the somesthetic senses, both of the skin and beneath the skin, to the question of feeling.

There is one very specific proposal along this line that is worth some thought. It has been offered by Nafe and is called the *quantitative theory of feeling*. The proposal is that pleasantness and unpleasantness in experience are related to the brightness and dullness of sensory experience. 'Pleasantness,' he suggests, arises from 'bright' experiences, like those that give us a 'thrill,' 'unpleasantness' from the dull or deep sensations. The theory makes some common sense, and there may be something to it. There are, however, relatively few experimental facts to support it or to deny it, so we should not spend much time on it.

Feeling and Autonomic Responses. Another notion, not tagged with any particular name, has been the subject of more experimental work. It is that pleasantness and unpleasantness are set apart by the division of the autonomic system that is most dominant. According to the hypothesis, sympathetic responses give rise to unpleasant experience; parasympathetic activity arouses pleasant experience. This view fits in fairly well with what we have already learned about deep pain, but let us examine more specifically some of the facts bearing on it.

There is quite a list of *parasympathetic* activities that, everyone will admit, go along with 'pleasantness.' One is the physiological response to warmth. This is the mild expansion of blood vessels, a parasympathetic response. Another is the secretion of saliva when we anticipate food and the secretion of gastric juices in hunger and digestion. The sexual act, urination, and defecation are usually pleasant and are primarily controlled by the parasympathetic system.

Besides these common-sense arguments, there are some experiments designed specifically to test the point (see Landis). One is the measurement of the blood volume of, say, the hand or finger under different conditions of pleasantness and unpleasantness. Increase of blood volume is a parasympathetic function, a decrease in it is a sympathetic result. This kind of experiment has been done a number of times with different situations to produce pleasantness and unpleasantness. Most of the experiments support the idea of a correlation. A few do not. These should not be taken too seriously, however, because the parasympathetic system, as we saw earlier (page 32), is rather specific in its activities, and the experimenters may have been looking in the wrong place for the expected changes in blood volume.

There is also some evidence that sympathetic discharge is correlated with 'unpleasantness.' A simple way of mimicking such discharge is to inject the hormone adrenalin. As you know, this constricts blood vessels, raises blood pressure, and does other things characteristic of the sympathetic system. When people are given adrenalin and asked 'how they feel,' they usually report that they feel 'stirred up' and 'tense' and 'unpleasant' as they would when they are afraid or angry. Sometimes, however, they report 'joy' or excitement that is pleasant. The experiment, therefore, does not give a clear result.

Conclusion. As you can see, the experiments on the question of pleasantness and unpleasantness are not very satisfactory. There are many difficulties in getting at such a question as this one. In the meantime, however, what we know about the sensory basis of pain may be as good to go on as anything. We know that changes in blood vessels brought about by chemical factors or changes in blood pressure and tension in muscles can both bring about feelings of pain or discomfort. We should not be going too far, therefore, if we say that these changes can be the basis of anxiety and unpleasant feelings; and we may tentatively believe that the opposite changes, those relieving or avoiding pain, may be pleasant.

THE KINESTHETIC SENSE

We shall come shortly to the central centers and pathways concerned in somesthesis. Before we do, however, there is still one somesthetic sense that we must take up briefly. This is kinesthesis. The receptors for this sense are to be found in the muscles, tendons, and joints. Although we are seldom aware of them, they are important. Unlike the skin receptors, which are stimulated now and then by energy from outside the body, the kinesthetic receptors are always being stimulated from within the body. Indeed, they are involved in our every movement.

The Kinesthetic Receptors. Besides free nerve endings in our blood vessels, there are three main types of kinesthetic end organs: the muscle spindle, the Golgi tendon organ, and the Pacinian corpuscle.

The *muscle spindle* is a somewhat complicated structure found in the equatorial region of muscles. As you can see in Fig. 102, it consists of muscle fibers innervated by sensory nerve endings—all enclosed in a tissue fluid and a capsule of connective tissue. Within the muscle spindle are nerve endings of two types, each named more or less according to its appearance: (1) the annulospiral endings and (2) the flower-spray endings. The annulospiral endings are the terminals of large fibers arranged spirally around the muscle fibers. The flower-spray endings are terminals of smaller, less myelinated fibers, which end in spraylike arborizations upon the muscle fibers. Both these receptors are so arranged that they are stimulated when the muscle stretches. For that reason they are called *stretch afferents.*

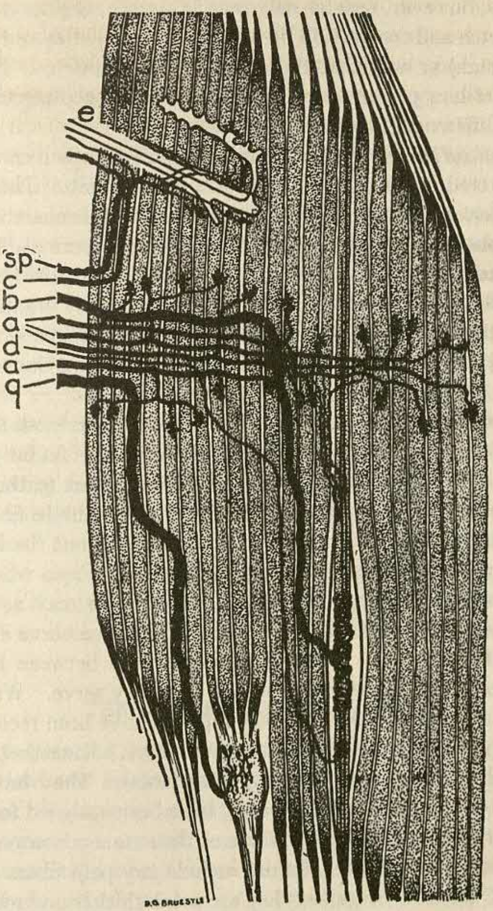

FIG. 102. Diagram of the sensory and motor innervation of muscle. Motor fibers, *a*, ending on various muscle fibers; *b*, annulospiral ending terminating in the muscle spindle; *d*, flower-spray ending also terminating in the muscle spindle; *g*, sensory fiber serving a Golgi tendon organ; *sp*, a sympathetic plexus serving the blood vessel, *e*, and accompanied by a sensory pain fiber, *c*. (*After Denny-Brown. From J. F. Fulton. Physiology of the nervous system. 2d ed. New York: Oxford,* 1943. *P.* 7. *By permission of the publishers.*)

The *Golgi tendon organs* are very specialized structures. You can see them in Fig. 102 around a few muscle fibers at their ends where they form a junction with the tendons. Innervating these organs are nerve endings, called simply tendon endings. These are stimulated by either an increase or a decrease of tension at the tendon-muscle junctures. In fact, these endings probably cannot distinguish between muscle contraction and muscle stretching. Because the muscle spindles, however, register only muscle stretch, the nervous system can distinguish stretch and contraction by whether both spindles and tendon organs are active (stretch) or only the tendon organs (contraction). This is just one more example of how patterns of activity in specific receptors tell the nervous system about differences in kind of stimulation.

The *Pacinian corpuscles* are structurally similar to other encapsulated end organs encountered in the skin, *e.g.*, the Krause end bulb. The Pacinian corpuscles, however, are generally much larger than cutaneous encapsulated organs. They consist of a capsule made up of several layers of fibrous tissue in which nerve endings ramify. They are distributed widely in the body: in the sheaths of tendons and muscles, in the linings of various organs of the body, and in the subcutaneous adipose tissue. They are organs of deep-pressure sensitivity and are excited by deformation of the tissue in which they are housed. They are served by large myelinated fibers.

Free nerve endings are also kinesthetic receptors—at least they tell us of events deep within the tissues and muscles of the body. As far as the muscles are concerned, however, free nerve endings are restricted to the blood vessels that serve the muscles; they do not end directly on muscle fibers. Unfortunately, we do not know as much as we would like to about the free nerve endings, how many there are, and just where they end. From what we know of pain arising from deep within the body, however, we may assume that the tendons and joints are especially well supplied with free nerve endings.

Kinesthetic Fiber Types. There is a nice relation between types of kinesthetic nerve fibers and the receptor organs that they serve. We have learned that from experiments in which nervous impulses have been recorded in nerves while the receptors are stimulated in various ways. Kinesthetic nerve fibers can be divided into four main groups (Matthews). They have been called A_1, A_2, B, and C. These letters, however, have been assigned for convenience; they do not correspond to A and C fibers of the cutaneous nerves. The A, B, and C kinesthetic fibers, in fact, do not include any pain fibers comparable to the cutaneous C fibers. Altogether they are much thicker and more myelinated and conduct impulses faster than the average fibers from the skin receptors. Let us consider each of the kinesthetic fiber groups in turn.

The A_1 and A_2 fibers are associated with the flower-spray endings and annulospiral endings, respectively. They are very similar in their properties except that the A_2 fibers conduct more rapidly and have larger diameters than the A_1 fibers. Because they innervate the muscle spindles, the A_1 and A_2 fibers are called stretch afferents. When the muscles that they serve are in their normal state, *i.e.*, nearly but not entirely relaxed, they discharge impulses at a slow rate of 5 to 15 impulses per second. Their rate of discharge quickly increases, however, the moment the muscle is stretched, say, by the contraction of an antagonistic muscle, and it may reach a level as high as 500 impulses per second.

B fibers have a higher threshold than the A_2 or A_1 fibers, they conduct more slowly, and they have smaller diameters. They are believed, upon good evidence, to serve the Golgi tendon organs. Their rate of response—nervous impulses—is increased by either active contraction or passive stretch of the muscles. The number of impulses per second that they produce is proportional to the *logarithm* of the tension exerted by the muscle. Thus the *B* fibers can be called *tension recorders*.

C fibers are associated with Pacinian corpuscles, for responses in them disappear when the muscle sheaths containing Pacinian corpuscles are dissected away. These fibers are somewhat smaller and slower than the *A* or *B* fibers.

Deep-pain fibers are not included in the *ABC* scheme for kinesthetic receptors. We can see free nerve endings in the vicinity of muscles, and subjective experience tells us that there must be such pain receptors in this region—muscles do get sore and hurt sometimes. Pain fibers were undoubtedly present in the nerves studied in the experiments with *A*, *B*, and *C* fibers, but being much smaller and giving much smaller impulses, their activity could not show up among the records of large impulses from the *A*, *B*, and *C* fibers. At any rate, it is fair to assume that small and mostly unmyelinated fibers having free nerve endings serve the experience of pain. It is also probable that such pain receptors are mostly, if not exclusively, distributed to blood vessels and to sheaths of muscles and tendons, rather than directly to muscle fibers.

THE SOMESTHETIC PATHWAYS

In the last chapter and up to now in this one we have been dealing with the peripheral somesthetic mechanisms—with what goes on outside the central nervous system. We are interested, of course, in the central mechanisms of somesthesis, too, and we are now ready to come to grips with them. In order to do that we must take a brief excursion into neurology and describe the general outlines of somesthetic centers and pathways.

The Dermatomes. One of the chief features of vertebrate animals is that their bodies, and particularly their bony structures, are divided into segments. You can see that most easily in fishes. In the higher vertebrates, such as the rat and man, it is a bit harder to see the segments, but they are there and are especially prominent in the very early stages of the embryo. Even in the adult, the vertebrae and spinal nerves are spaced in fairly regular segments. Each spinal nerve represents a segment or *metamere* in the embryo, and although the body itself has lost a segmental appearance, the spinal nerve serves a limited area of the body. This area is called a *dermatome*. Each dermatome, in the human adult, is somewhat irregular in shape and size, but the position

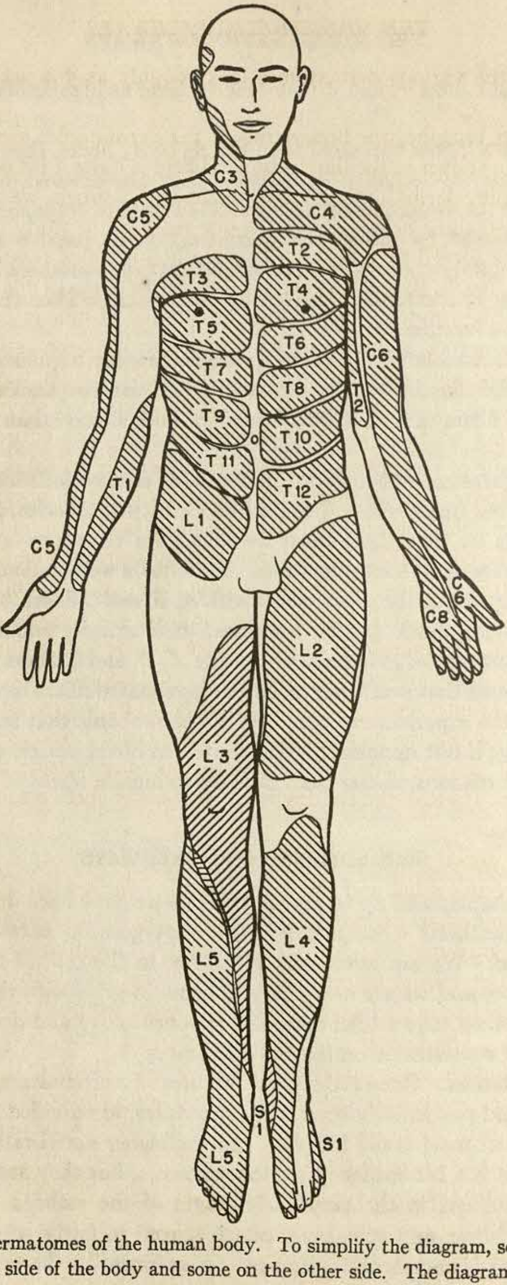

FIG. 103. The dermatomes of the human body. To simplify the diagram, some dermatomes are drawn on one side of the body and some on the other side. The diagram is based on the skin sensibility that remains after injury to different nervous pathways of different spinal segments. The letters stand for regions of the cord represented: *C*, cervical; *T*, thoracic; and *L*, lumbar. The numbers refer to particular segments of the spinal cord. (*From T. Lewis. Pain. New York: Macmillan*, 1942. *P.* 20. *By permission of the publishers.*)

and shape of the various dermatomes look roughly as you see them in Fig. 103.

As you might imagine, the boundaries of the dermatomes are not really as clear as they are shown in the illustration. There is quite a bit of overlapping. In fact, in mapping dermatomes in experiments with animals, we must cut three nerves below and three nerves above the one we want to study in order to determine the area served by a nerve. This method is called the method of "remaining sensibility." By such a method, the dermatomes of the monkey have been mapped (Sherrington). By taking advantage of human cases with sections of various nerves, a similar map for man also has been assembled.

Figure 103 can show only the map for the skin. Under the skin there is a similar grouping. In fact, fibers of the same nerves that serve the skin also go to the muscles, tendons, joints, and deep tissues. The entire distribution, regardless of type of receptor, is divided up in terms of spinal segments.

The Spinal Roots. As we follow the somesthetic nerves inward toward the spinal cord—we shall consider the face and head later—we find that just before we reach the cord, all the nerves from a body segment join together in one nerve (see Fulton). Thus the fibers for pain, temperature, and pressure and from the skin, muscles, and deep parts of the body get together in one bundle to enter the cord. In fact, for a short distance outside the cord both the motor and the sensory fibers are joined in one nerve. On approaching the cord, however, they divide into sensory and motor roots. The somesthetic fibers make up the dorsal root and the motor fibers the ventral root. And as we noted back in Chap. II, all the cell bodies of the *sensory* fibers lie outside the cord in the dorsal ganglion, whereas the cell bodies of the *motor* fibers are inside the cord in the ventral horn.

Between the dorsal ganglion and the cord itself, the sensory roots divide into two filaments, one medial and the other lateral. The medial filament goes to the dorsal column of white matter (fibers) and the lateral filament goes to the dorsal horn of gray matter (chiefly cell bodies). This division has functional significance. The medial filament has mostly large myelinated fibers and, as you might guess from this fact, represents pressure receptors, both kinesthetic and cutaneous. The lateral filament, on the other hand, is made up of the smaller fibers, unmyelinated and lightly myelinated. It has in it the fibers from the pain and temperature receptors, both deep and cutaneous. So you see, at this point the fibers divide, not according to skin or muscle or tissue from which they came, but according to the kinds of receptors they serve. All the fibers, after they get into the cord, divide and send branches both upward and downward in the cord.

The Spinal Cord. The relations of various tracts and nuclei of the somesthetic system are known quite well. The matter, however, is rather complex, and in the space we have to give it here we cannot be completely accurate. What we say, then, is true in general but not in every detail. Moreover, to make the pathways clear we need two illustrations, one for the skin senses and the other for kinesthesis. Otherwise the diagrams would be too cluttered to read. In what follows, therefore, you should refer to Figs. 104 and 105, whichever is appropriate.

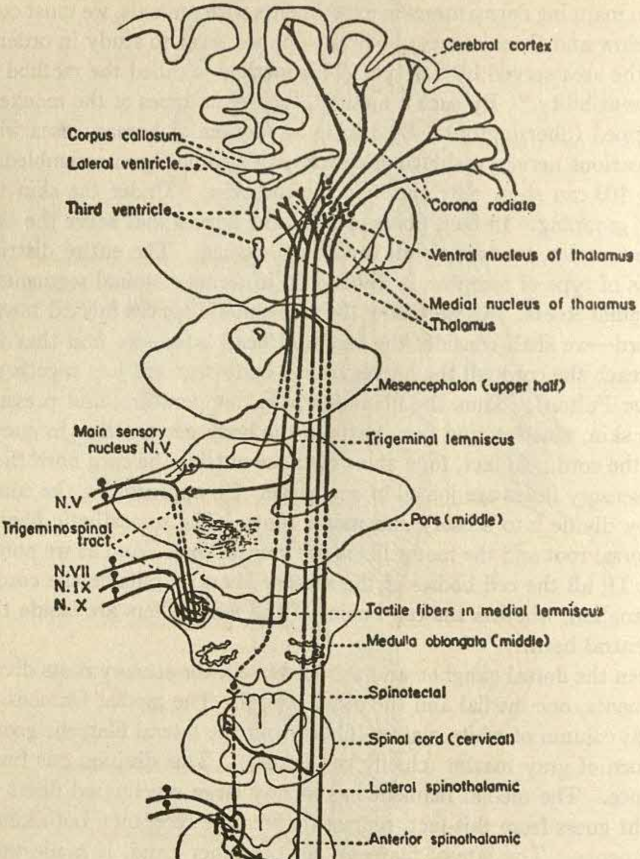

FIG. 104. Diagram illustrating the chief centers and pathways of the cutaneous sensory system. (*From A. Kuntz. A textbook of neuroanatomy. 4th ed. Philadelphia: Lea & Febiger, 1945. P. 214. By permission of the publishers.*)

Many of the fibers from both medial and lateral filaments do not go very far once they get into the cord. These are concerned in one way or another with various spinal reflexes. A few fibers may go directly to the ventral horn cells, where they make synapse directly with motor cells to effect the simplest reflexes. Others end on internuncial cells in the gray matter of the cord, and the internuncials make reflex connections with the motor cells. These connections can, of course, involve more than one level of the cord. Since they are concerned with reflexes, which we shall come to in a later chapter, rather than with sensory experience, we shall pay no more attention to them here. Instead, let us turn to the ascending tracts and consider them according to the filament from which they arise.

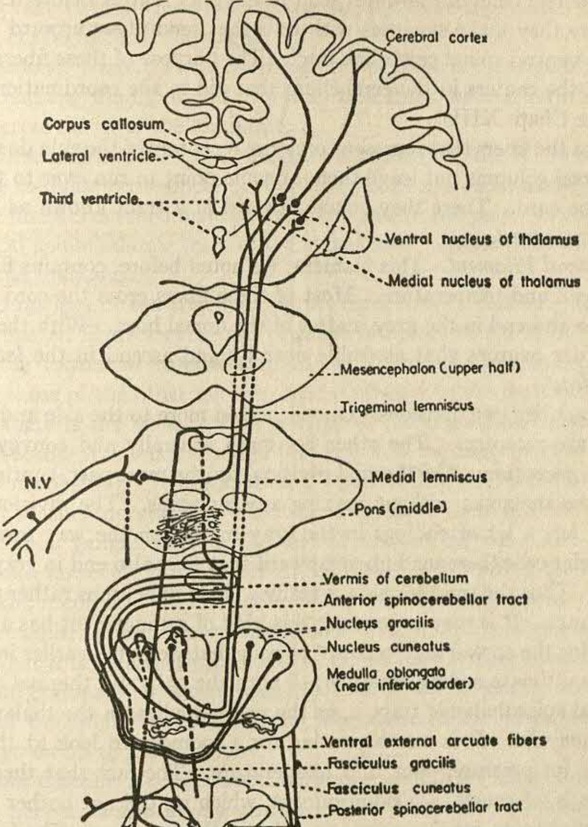
Cerebral cortex
Corpus callosum
Lateral ventricle
Third ventricle
Ventral nucleus of thalamus
Medial nucleus of thalamus
Mesencephalon (upper half)
Trigeminal lemniscus
N.V
Medial lemniscus
Pons (middle)
Vermis of cerebellum
Anterior spinocerebellar tract
Nucleus gracilis
Nucleus cuneatus
Medulla oblongata (near inferior border)
Ventral external arcuate fibers
Fasciculus gracilis
Fasciculus cuneatus
Posterior spinocerebellar tract
Anterior spinocerebellar tract
Spinal cord (upper thoracic)

FIG. 105. Diagram of the centers and pathways of the kinesthetic system. (*From A. Kuntz. A textbook of neuroanatomy. 4th ed. Philadelphia: Lea & Febiger, 1945. P. 212. By permission of the publishers.*)

The Medial Filament. This, you will remember, represents pressure receptors, both kinesthetic and cutaneous. Fibers enter the dorsal (posterior) columns, run upward for some distance, and then cross over to the opposite side of the cord. On each side of the cord there are two dorsal columns, called *gracilis* and *cuneatus*, respectively. Many kinesthetic fibers remain in the columns and ascend upward without making any synapses until they get to the *gracile nucleus* and *cuneate nucleus* of the medulla. Some kinesthetic fibers from the dorsal columns, however, end in the gray matter before they go very far. There they make synapses with cells that send fibers upward in another tract, the ventral spinal cerebellar tract. The purpose of these fibers is to connect with the centers in the cerebellum that aid in the coordination of movements (see Chap. XIII).

Many of the fibers that represent pressure receptors of the skin do not remain in the dorsal columns but leave them at some point to run over to the ventral part of the cord. There they course upward in a tract known as the *ventral spinothalamic tract.*

The Lateral Filament. This filament, we noted before, contains fibers representing pain and temperature. Most of these fibers cross the cord as soon as they enter and end in the gray matter of the dorsal horn. With them connect second order neurons that assemble near by and ascend in the *lateral spinothalamic tract.*

This tract has two divisions. One is located more to the side and represents temperature receptors. The other lies more ventrally and conveys impulses from pain receptors. The thermal division, for the most part, continues all the way to the thalamus without making any synapses. The division for pain, however, has a lot of endings in the gray matter on the way upward. The higher order cells there send fibers upward that may also end in gray matter of the cord. Thus the tract for pain is really a chain of neurons rather than a continuous tract. It is easy to see how this kind of arrangement has a lot of possibilities for the spread and 'mix-up' of pain that we noted earlier in this chapter. The ultimate ending, however, of both the pain and thermal divisions of the lateral spinothalamic tract is, as the name implies, in the thalamus.

Syringomyelia. It is worth pausing for a moment to look at the different pathways for pressure, pain, and temperature. The fact that there are such pathways is, of course, a good argument, which we did not bother to mention in the last chapter, for the specific function of the receptors. The fact has been established in various ways. One of them is what happens in a disease called syringomyelia. This disease starts in the central gray matter of the cord and spreads outward. In its course, one sees different degrees of impairment of somesthetic experiences. The first to be lost is pain. When it is almost gone, there may be little or no impairment of pressure and thermal sensitivity. Next to go is temperature. Finally, when the disease is well along, pressure sensitivity also drops out. The order of progress does not follow as neatly as this in every case, but it is a general enough rule to mean something.

The Hindbrain. Now let us move on to the centers of the brain. The spinothalamic tracts of the spinal cord keep on going upward until they reach the thalamus. But in the hindbrain (medulla and pons) there are two additions to the system. One is the addition of pathways for the head and face. The sensory tracts of the spinal cord serve only the trunk and limbs. Somesthetic impulses from the head come in directly to the brain over cranial nerves. Several nerves take part in this pathway, among them the trigeminal, the facial, the glossopharyngeal, and the vagus.

The Trigeminal Nerve. The most important of these is the trigeminal nerve. Upon approaching the hindbrain it divides into three main roots which go to their respective nuclei of the hindbrain.

One of these nuclei is the *spinal nucleus*—so called because it extends downward in the medulla to the upper part of the spinal cord. This nucleus receives the smaller fibers concerned mainly with temperature and pain. It corresponds to the lateral spinothalamic tract of the spinal cord. Axons from this nucleus ascend to the thalamus.

A second nucleus of the trigeminal is the *chief sensory nucleus.* It gets the larger myelinated fibers serving the pressure receptors of the skin. It corresponds to the ventral or anterior spinothalamic tract of the spinal cord. Its axons, like those of the other nucleus, course upward to the thalamus.

Finally, there is the *mesencephalic nucleus* of the trigeminal nerve. It has this name because it extends through the pons into the lower part of the midbrain (mesencephalon). It has another distinctive feature, too. Most spinal and cranial sensory nerves, you will remember, have their cell bodies in the dorsal or cranial ganglia outside the central nervous system. The mesencephalic nucleus, however, is an exception. Although it lies within the hindbrain and midbrain, it contains the cell bodies of first-order sensory fibers. The final point to remember about the mesencephalic division and nucleus of the trigeminal is that it is kinesthetic in function. It serves the muscles and joints of the head and cranium. It is comparable, therefore, to the gracile and cuneate pathways of the spinal cord. Its axons, like those of the other somesthetic pathways, go on up to the thalamus.

Gracile and Cuneate Nuclei. The hindbrain, aside from these inputs from the cranial nerves, is also a way station for the kinesthetic pathways of the spinal cord—the gracile and cuneate tracts. In the medulla are two nuclei, the gracile and cuneate nuclei, and it is in these nuclei that the long kinesthetic fibers of the dorsal columns end. In these nuclei are the cell bodies of second-order neurons that send axons up to the thalamus.

CENTERS OF THE FOREBRAIN

You will note in this discussion so far that the tracts and nuclei of both the spinal cord and hindbrain are so segregated that different kinds of impulses are, for the most part, kept in different tracts. The kinesthetic impulses travel in the gracile, cuneate, and mesencephalic pathways. The touch impulses from the skin run in the ventral spinothalamic tract and the chief sensory pathway of the trigeminal, and the pain and temperature impulses run in the lateral spinothalamic and the spinal division of the trigeminal.

The Thalamus. When all these pathways reach the thalamus, however, there is no longer any segregation according to function. In fact, impulses from the taste pathways also join the procession and end in the same nucleus of the thalamus. That nucleus is the *posteroventral nucleus*. It shows no separate parts for pain, temperature, pressure, or taste. Instead it is arranged—so far as we know now—on a purely topographical basis. One part of it represents all somesthetic senses of the legs, another the same senses of the arms, and still a third part the face. This last part, because it is relatively larger and more important, has its own special name, the *arcuate nucleus*, although it is part of the posteroventral somesthetic nucleus.

The Somatic Cortex. We have said many times that the thalamus is a relay station. That is what it is in the somesthetic sense as well as in other senses. The relay functions may not be so simple as we once thought they were, but they are, nevertheless, relays. For that reason it is better now to go on to the cortex and to bring in the relay functions of the thalamus as they are needed to understand the cortex. There have been two principal methods in tracing thalamocortical functions, the method of anatomic projection and that of evoked potential. We shall discuss them in turn.

ANATOMICAL PROJECTION

The posteroventral nucleus of the thalamus projects upward to the postcentral gyrus of the cortex (see Fulton). In animals below primates, such as the rat or rabbit or cat, where there is no true central sulcus and consequently no true postcentral gyrus, the projection is nevertheless to an area corresponding to the postcentral gyrus. In primates, we often refer to this area in the Brodmann number system as area 3–1–2.

Primary Projection. The area is laid out topographically (see Fig. 106). At the top near the longitudinal fissure is the leg area. Then below it and more to the side is the arm area. In between is a small strip for the trunk. Then, far to the side, toward the temporal lobe, is the face area. This gets projections from the arcuate portion of the posteroventral nucleus. The relative space given to these different areas does not correspond with the size of the parts of the body but rather to the relative importance of these areas in somatic functions. Thus in higher animals such as the primates, the face is given much more space on the cortex than the arm or leg.

'Associative' Projection. By the method of tracing anatomical projections, one can distinguish a second relay from the thalamus and a second area of the cortex. The relay occurs through the *lateral nucleus* of the thalamus, which sends its dendrites to the posteroventral nucleus and its axons to the cortex.

This relay is shown in the diagram in Fig. 16 that we looked at back in Chap. III. The receiving area of the cortex for this relay is back of the postcentral gyrus. Its limits are not well defined, but for practical purposes we may consider it to be the *posterior parietal lobule*, the major part of the parietal lobe other than the postcentral area.

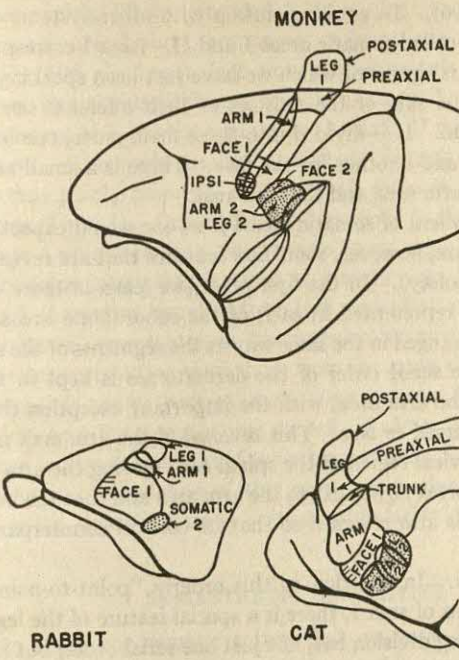

FIG. 106. Diagrams of the somatic areas of the cortex in the rabbit, cat, and monkey. In each diagram the dotted area is somatic area II. In every case area II can be subdivided roughly into face, arm, and leg areas, but the diagram for the rabbit is too small to show that fact. There is a certain amount of overlapping of face, arm, and leg subdivisions in both area I and area II. The crosshatched part of the face area I in each diagram is the part that has ipsilateral representation of the face. Note that somatic area II is located laterally toward the temporal lobe, not in the posterior parietal lobule. (*Based on Woolsey*, 1947, *but modified and completely redrawn.*)

FUNCTIONAL ORGANIZATION

For reasons that are not too clear as yet, we get a different picture of the somatic cortex if we map it with an electrical method rather than an anatomical method. In the electrical method, you will remember from Chap. III, electrodes are placed at different positions on the cortex while different sense organs or sensory nerves are being stimulated. This method tells us a number of things about the somatic cortex that are probably more meaningful functionally than are the anatomical facts (see Woolsey; Adrian; Woolsey *et al.*).

Somatic Area I. The electrical method reveals two main somatic areas in the cortex (see Fig. 106). To avoid confusion with other systems of naming, these areas have been called somatic areas I and II. Area I corresponds fairly well with the postcentral gyrus of which we have just been speaking. It gives potentials whenever the skin or the muscles or their afferents send impulses into the nervous system. It is divided into three main parts, one for the legs, another for the arms, and another for the face. There is a small area for the trunk in between the arm area and the face area.

The general arrangement of somatic area I is as one would expect from anatomical data. There are, however, some new features that are revealed by the electrical method (Woolsey). In the first place, we learn in more detail how parts of the body are represented in each of the subordinate areas. The leg area, for example, is arranged in the same way as the segments of the spinal cord serving the skin. The serial order of the dermatomes is kept in the cortex. The same is true for the arm area, with the important exception that the entire serial order is reversed *en bloc*. This reversal of the arm area means that the top part of the cervical region of the spinal cord serving the arm and trunk is represented in the cortex right next to the arm area and that the bottom part of the cervical region is also reversed so that its cortical counterpart lies next to the face area.

Axial Representation. In addition to this orderly "point-to-point" projection within the divisions of area I, there is a special feature of the leg area that is worth a note. The leg division has, not just one serial order, but rather two, one for the front of the leg and the other for the back. The part of the leg area right at the top of the postcentral cortex is for the front of the leg from hip to toes, and the part down in the longitudinal fissure is for the back of the leg from toes to hip.

Ipsilateral Projection. The main projection in somatic area I is contralateral—one side of the body is projected to the opposite cortex. In addition, however, the electrical method shows that there is also an ipsilateral representation of the face—and the face only—lying just in front of the main face area. This has been given the name *ipsilateral face area* as an additional subdivision of area I.

Precentral Kinesthetic Projection. If, in the process of stimulation, kinesthetic receptors or nerve fibers are added to those of the skin, potentials appear not only in the postcentral cortex but also in the *precentral cortex*. This we have already seen is a motor cortex. It is the area from which motor impulses go down to the spinal cord and out to skeletal muscles. In regard, therefore, to kinesthesis, area I also includes the motor or precentral cortex, whereas for the skin senses it consists only of postcentral cortex. We can imagine that the projections are arranged in this fashion so that kinesthetic impulses can help directly in motor coordination.

Somatic Area II. As you might expect, there is a second somatic area. That area, however, as revealed by electrical methods, does not correspond to the posterior parietal lobule. Instead, it lies on the lateral surface of the cortex between somatic area I and the temporal auditory area. This area II, as you can see in Fig. 106, also has its face, arm, and leg sectors. They have been laid out, however, in a slightly different way than in area I. The face area of II is near the face area of I, but the arm and leg areas of II lie to the rear toward the auditory area. The positions are somewhat different for different animals. The important point, however, is that in all animals there are two distinct somatic areas, I and II. One of them corresponds to the postcentral area, but the other has a unique position near the auditory area.

There are some interesting features of somatic area II. In the first place, unlike area I, it receives impulses from *both sides* of all parts of the body. Despite this bilateral representation, the impulses from the opposite side of the body are better represented than those from the same side—at least, they give cortical potentials about twice as large. Somatic area II also seems to be not only a sensory area but a motor area as well. At least, it lies in a position that has long been known to be a part of the extrapyramidal motor system (see Chap. XIII). Electrical *stimulation* of this area can produce small movements of face, arm, or leg, depending on the site of stimulation (see Woolsey).

SOMESTHETIC SENSITIVITY

The facts about the somatic cortex that we have just gone over are relatively recent. With them in hand it is possible to do very careful experiments on the cortical basis of somesthetic experience. There has not yet been time, however, to do the various experiments that would seem fruitful. So at present what we have in the way of psychological experiments does not make use of the facts of electrical recording. And what we know is not very satisfying. What there is of it, however, can best be explained by considering the different animals that have been used in experiments.

The Rat. We know practically nothing about the cortical mechanisms of kinesthesis in the rat. There is some hope that in the next few years we will. The situation with respect to tactual discrimination is almost as bad, but there is one experiment worth reporting (Smith). Rats were given the problem of discriminating the roughness of two sandpapers. After they had mastered the discrimination, lesions were made at various places in their cortices. When the lesions were made in certain areas their memory for the discrimination was partly or wholly destroyed. In all cases, however, they were able to learn the discrimination again if given a fair number of relearning trials. This fact leaves us not knowing whether it was a basic sensory mechanism of the cortex that was affected or rather some capacity having to do only with the memory for discrimination (see page 465).

Monkeys. We have some studies of kinesthesis in monkeys before and after the removal of some cortical areas (Ruch). The monkeys were taught to discriminate differences in weights. The areas removed in the animals were different combinations of the precentral (motor), postcentral (area I), and posterior parietal areas. This is what happened:

When the postcentral area (I) was removed on both sides, there was no harm done to weight discrimination. Neither was there when the precentral (motor) area was taken out. In fact, when rather large lesions invading both the pre- and postcentral areas were made, nothing happened to weight discrimination. This experiment, however, has its shortcomings, because the investigators could not take out completely both precentral and postcentral area, for that would produce a motor paralysis that would interfere with the discrimination.

What did produce some loss in discrimination was the removal of both the postcentral area (I) and the posterior parietal lobule. After this operation the animals needed a much larger difference in weights to discriminate them than they did before. Postoperative training helped efface the impairment to a certain extent but did not by any means bring the animals back to their preoperative level of performance. From this experiment we can conclude that the first somatic area (I) is not by itself responsible for kinesthetic discrimination, but that it, together with the posterior parietal lobule, plays some part in it. None of the operations, however, invaded somatic area II, and we do not know therefore what role this area may play in the capacity.

Chimpanzee. The same sort of experiments have been carried out with the chimpanzee (Ruch *et al.*). In this case, too, there were both tactual and kinesthetic discriminations. Because the chimpanzee is difficult and expensive to get for experimental purposes, the experiments are not exhaustive. They suggest, however, that the cortex of the chimpanzee is more important in kinesthetic discriminations than that of the monkey. In Fig. 107 you see a summary of the results in one chimpanzee as well as the operations that were performed on the animal.

Weight Discrimination. When the postcentral area (somatic I) was removed there was some impairment in weight discrimination. The impairment was slight, however, and it was effaced by giving the animal further training. Removal of the posterior parietal lobule, on the other hand, caused much more severe losses in weight discrimination. These improved after some rest and retraining, and eventually the animal returned almost to normal. Finally, parietal lobectomy, *i.e.*, removal of both the postcentral area and the posterior parietal lobules, caused a profound impairment. This could not be effaced by retraining, although it did improve a bit. Putting together all these results would lead us to believe that the posterior parietal lobule in the chimpanzee is more important in kinesthetic discrimination than the postcentral area (somatic I) but that both contribute to the ability. Note again that this experiment tells us nothing about the role of somatic area II, which was not known at the time of the experiments.

Tactual Discrimination. Now let us summarize the experiments with tactual discrimination. Discriminating roughness was one of the tasks given to chimpanzees. Another more complex tactual task was to discriminate form tactually (stereognosis), say, by picking a cone from a cone and pyramid or selecting a pyramid from a pyramid and wedge. Removing the postcentral area did no harm to roughness discrimination. Taking out the posterior parietal lobule, however, caused some deficit in discrimination that was not very serious. Even greater impairment followed removal of the parietal lobe, *i.e.*, postcentral and posterior parietal areas together.

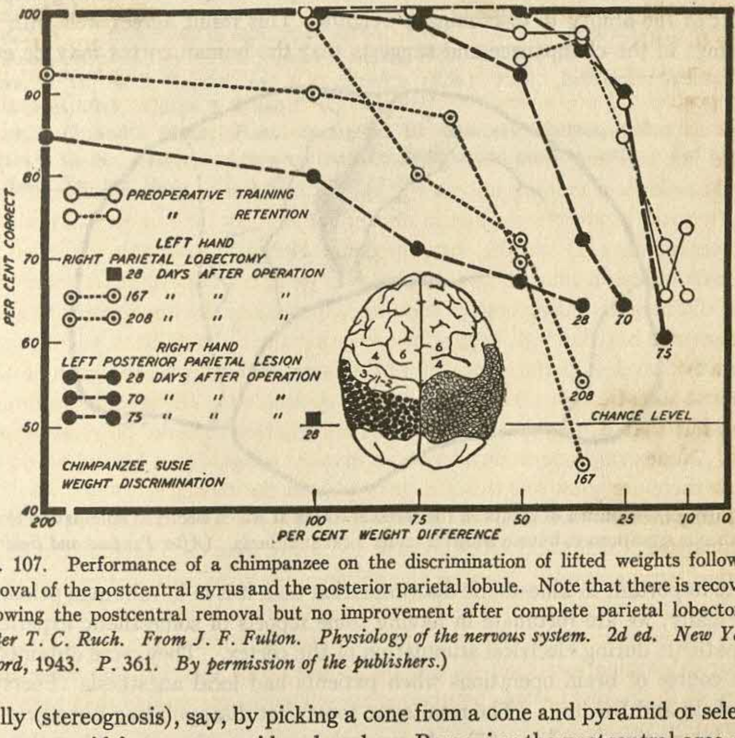

FIG. 107. Performance of a chimpanzee on the discrimination of lifted weights following removal of the postcentral gyrus and the posterior parietal lobule. Note that there is recovery following the postcentral removal but no improvement after complete parietal lobectomy. (*After T. C. Ruch. From J. F. Fulton. Physiology of the nervous system. 2d ed. New York: Oxford,* 1943. *P.* 361. *By permission of the publishers.*)

The serious losses from operations like these, however, were seen, not in simple roughness discrimination, but rather in the stereognostic (form) discrimination. This kind of discrimination was completely lost after removal of the posterior parietal area. Some, but not all, of the capacity was recovered in time. But the animal never learned to distinguish a pyramid from a wedge, although it did recover the ability to tell the difference between a cone and a pyramid.

Man. It is seldom possible to make careful studies of the effect of brain lesions in man. In the case of kinesthetic (weight) discrimination, however, we have some measurements comparable to those we just described for the monkey and chimpanzee (Ruch *et al.*). These were made in two patients in whom rather precise surgical lesions were made. One patient had a lesion in the anterior (postcentral) part of the parietal lobe and the other in the posterior parietal area. Both patients showed pronounced and lasting impairment of the ability to discriminate weights. This result agrees well with the findings in the chimpanzee and suggests that the human cortex may be even more important in kinesthetic discrimination than it is in infrahuman primates.

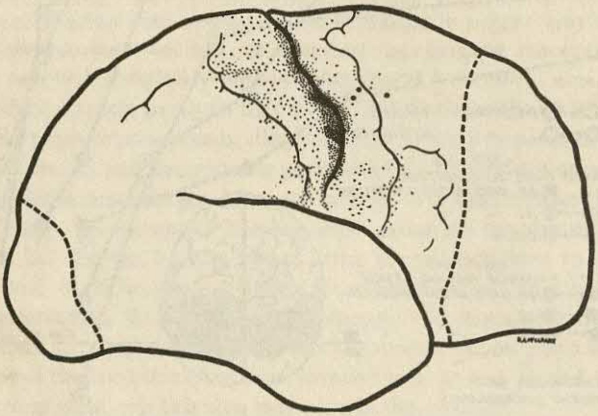

FIG. 108. Distribution of points on the cerebral cortex at which electrical stimulation evokes cutaneous sensations in human subjects under local anesthesia. (*After Penfield and Boldrey.*)

Finally, we are fortunate in having some reports of somesthetic experience in patients during electrical stimulation of the cortex. They were obtained in the course of brain operations when patients had local anesthesia (Foerster; Penfield and Boldrey). The results are somewhat disappointing but nevertheless interesting (see Fig. 108). As you might expect, they show that the precentral and postcentral areas are arranged to represent different parts of the body. A stimulus, for example, in the dorsal leg area is reported by the patient as in his leg. This fits with what we already know from other methods. It is interesting, too, that somatic experience can be aroused in patients when the posterior parietal areas are stimulated, but the intensity of the stimulus must be higher.

As one might expect also from the anatomical and physiological data, there is no segregation of experiences in different areas. Different types of experience are reported from stimulation in the same areas. With the kinds of electrical stimulation used so far, however, sensations of pain, warmth, or cold were very rarely reported. More common were sensations of numbness, tingling, or movement. Perhaps this was due to the kind of electrical stimuli used. At any rate, we do not yet have any knowledge of how the different types of somatic experience are set apart from each other in the somatic cortical areas.

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CHAPTER XIII

THE MOTOR SYSTEM

The motor system for reflexes and coordination includes the striated muscles and centers and pathways at all levels of the nervous system from the cortex to the spinal cord. The best way of talking about the motor system is to work from the outside in—start with the muscles and go up through the spinal cord to the cerebral cortex. That, in general, is the outline for this chapter, although we shall depart from it occasionally where it makes good sense to do so.

NEUROMUSCULAR RELATIONS

A striated muscle is a group of muscle fibers gathered together in a bundle. This bundle is covered by sheaths of connective tissue, and it is also joined to bones by tendons of connective tissue. In some instances muscles are attached to each other. There are many muscles in the body, but there is no need to detail their names and positions here. Most important to note is the distinction between *flexor* and *extensor* muscles. This distinction holds primarily for the muscles of the limbs, but it applies also to some of the muscles of the neck and trunk which work together with the limb muscles. Flexor muscles, when they contract, lift limbs from the ground. Extensor muscles have the opposite effect—they push limbs toward the ground, thereby supporting the body.

The Motor Unit. Muscle fibers are served and controlled by neurons. The cell bodies of these neurons are in the ventral horns of the spinal cord or, in the case of muscles of the head, in the motor nuclei of the brain stem. From these places in the central nervous system, axons go out to the various muscles of the body. Just before reaching them, the axons divide into a number of axon fibrils (Eccles and Sherrington). Each axon fibril ends upon a muscle fiber, and each muscle fiber, it seems, usually gets only one axon fibril (Wiersma). Thus one motor neuron has complete control of a number of muscle fibers. A functional *motor unit*, therefore, is made up of one neuron and a number of muscle fibers. The several fibers of a motor unit may not be all together—they may be separated by muscle fibers or another motor unit—but they are nevertheless a unit because they are all served by one neuron.

The size of a motor unit varies from place to place in the body. How big it is is indicated by the *innervation ratio* (Clark). This is the ratio of muscle fibers to nerve axons. In some parts of the body the ratio is as high as 150:1, in others it may be as low as 3:1. And these ratios mean something, for you can see that an impulse in an axon fiber with a high ratio causes a relatively large contraction compared with that in an axon fiber with a small number of muscle fibers. Thus in the large muscles of the body that are used in walking and in large, crude movements, the ratio is quite high. In the small muscles, like those of the eye or the fingers, which make very fine adjustments, the innervation ratio is rather small. The innervation ratio, therefore, tells us something about the precision and fineness of movements.

Properties of Muscle Fibers. Just as a matter of background, we ought to consider briefly how muscles work. A nervous impulse arriving at the juncture between the axon and the muscle fiber is the stimulus for the muscle's activity. There has been some debate about what happens at the juncture. Some have thought that a chemical substance is secreted and intervenes in the process of excitation (see Feng), but another view, the electrical view, that the currents set up by the nervous impulse directly excite the muscle fiber, has come to prevail more and more. In fact, we now know that there is a local potential—just like that found at neuronal synapses, and indeed more prominent—aroused at the end place where the axon fibril and the muscle fiber join (Kuffler).

In brief, the events in muscle fibers seem to be the same in general outline as those in the somas of neurons of the central nervous system (see Young). First the action potential in the axon fibril arouses a local potential in the muscle fiber. This may build up to become big enough to set off a propagated disturbance, a spike potential, that is like that of neurons—all-or-none in size. In the wake of the spike potential are negative and positive after-potentials, and these complete the same cycle as that in neurons. All this occurs because muscle fibers, like nerve fibers, have polarized membranes whose equilibrium may be disturbed and cause both local and propagated releases of energy.

Unlike the nerve fiber, however, the muscle fiber does more than give action potentials—it contracts. This it does, not by shrinking or getting smaller, but by shortening and thickening. It changes its shape. And muscle physiologists now can tell us exactly how and why it does it (see Wilhelmi). The muscle fiber is made up of very large chemical molecules that are arranged in an orderly fashion. In contraction, the atoms making up these molecules are quickly rearranged so that the molecules, and thus the fibers, change in shape.

Red and White Muscle Fibers. Before we wind up this brief discussion of muscle fibers, we ought to note a fact about their structure that is also important in their function. In many muscles of the body, particularly the extensor muscles, there are two kinds of fibers, one red and one white (see Fulton). Red fibers have their color because they contain muscle hemoglobin—a rich source of energy. They also have stored in them large quantities of fat granules. Both these characteristics go along with an ability for long and sustained activity. White muscle fibers, on the other hand, lack such supplies of energy-rich materials needed for prolonged energy expenditure, and they therefore can function only for much briefer periods of time.

Related to these two kinds of muscle fibers are several facts of interest. In soaring birds, such as ducks, that can remain aloft for long periods, the muscles that are used in flying—the pectoral muscles—are made up largely of red fibers ("dark meat"). Birds, on the other hand, that seldom fly, *e.g.*, the chicken, have their flying muscles made up largely of white muscle fibers ("white meat"). Corresponding to this difference are differences in the properties of the white and red muscles. White muscle fibers contract much more quickly, they reach their highest tension in contraction more rapidly, and they relax to a normal resting state more rapidly than do red muscle fibers. Because they differ in what they can do, we find them involved in different kinds of behavior. It is the flexor muscles that make quick temporary adjustments, and these in general are white. The extensor muscles, on the other hand, are used for support and for long-sustained postures, and these tend to be red.

Speaking somewhat more generally, we may note that effectors are of two kinds, *phasic* and *postural*. The phasic effectors are for quickly executed temporary reactions, and the postural effectors are for sustained, longer lasting reactions. We shall come back to this distinction in the next chapter when we deal with the reflexes.

SPINAL MECHANISMS

So far in this book, we have been talking of the spinal cord as a great conducting mechanism that carries somesthetic impulses upward toward the brain and motor impulses downward to the various motor outlets of the spinal cord. It certainly is that, but it is also more than that. It is also a reflex mechanism that takes care of many responses without any aid from the higher centers of the nervous system.

We have already talked about the segmental structure of the spinal cord (page 259). This makes a good basis for distinguishing two varieties of reflex mechanisms in the spinal cord. Some mechanisms are segmental and others are intersegmental (see Lloyd, Fulton).

Segmental Arcs. Neurophysiologists talk about the neuron pathways that make up the reflex mechanisms as *arcs*. These arcs are made up of three parts: (1) incoming *sensory neurons*, (2) interconnecting, or *internuncial*, neurons, and (3) *motor neurons*, or motoneurons, leaving the spinal cord and going out to the muscles. Sometimes, but very rarely, there are segmental arcs that are made up of only two parts, the incoming sensory and the outgoing motor neurons. This is the monosynaptic arc, and it is the mechanism for a *monosynaptic reflex*. Much more typical, however, is the arc that includes the internuncial cell. The cell bodies of the internuncial neurons lie in the central gray matter of the spinal cord. When all three parts of the arc connect together at one segmental level of the spinal cord, the arc is a segmental arc. Later on, we shall see examples of reflexes that depend on such segmental arcs. Some such arcs are uncrossed, *i.e.*, all three parts are on one side of the spinal cord. There are, however, crossed arcs in which the internuncial neuron crosses from one side of the spinal cord to the other and the motor neuron is on the opposite side of the cord from the sensory neuron.

Intersegmental Arcs. These are formed when either the axons of incoming sensory neurons or the fibers of internuncial neurons travel up or down the segments of the spinal cord before making connection with a motor neuron (see Fulton). There is, in fact, a special tract called the *fasciculi proprii,* which lies near the gray columns of the spinal cord and connects various segments. This tract is made up of internuncial neurons. These intersegmental connections may be unilateral, *i.e.*, they may remain on the same side, or they may cross over the mid-line of the spinal cord to make a crossed intersegmental arc.

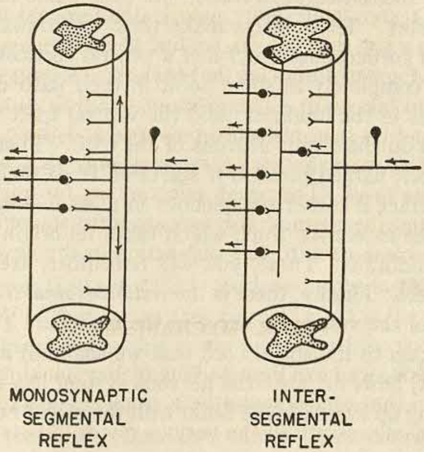

FIG. 109. Diagram of the neurons and synapses involved in segmental and intersegmental reflexes. On the left is a bipolar cell connecting directly with the motor neurons of the ventral horn of the same segment, as in the simplest segmental reflexes. On the right is diagrammed the internuncial path from a bipolar sensory neuron to the motor neurons of several segmental levels of the spinal cord. This is the kind of pathway involved in the scratch reflex. (*Redrawn after J. F. Fulton. A textbook of physiology. 16th ed. P.* 80.)

We shall come later to the description of various reflexes, but it may help to make clear here the anatomical basis of an intersegmental arc if we take a specific example, the "scratch reflex" of the dog. This is a reflex that we have all observed, and it is one that has been studied carefully by anatomical methods. The arc for this reflex is as follows: (1) Assuming that the stimulus is a tickling of the shoulder, a sensory neuron comes in from the skin of the shoulder to the corresponding segment of the spinal cord and ends in the gray matter of the segment. (2) Then a long internuncial neuron descends from that segment to the spinal segments for the hind limb. (3) This internuncial neuron connects finally with a motor neuron that goes out to the flexor muscle of the leg. You can see the connections that make up this arc in the diagram of Fig. 109. There are other intersegmental reflexes, and we shall describe them in the next chapter.

Descending Motor Tracts. The motor neurons of the spinal cord are not only a part of the spinal arcs that we have just described, but they also receive impulses from several motor tracts that start at various points in the brain and descend to the cord (see Ranson). The most important and most conspicuous of these tracts are the *corticospinal tracts*. As their name indicates, they arise in the cerebral cortex. These tracts make their way downward in two main divisions, a lateral corticospinal tract and a ventral corticospinal tract. Both these tracts cross completely at some point in their path downward, but the lateral tract crosses in the hindbrain and the ventral tract crosses in the cord just before it ends on the motor neurons of the cord. There is another tract, the *rubrospinal tract*, named because it starts off from the red nucleus of the hindbrain. This tract is rather conspicuous in most mammals. Another important tract is the *tectospinal tract*, which takes its origin in the tectum (or colliculi) of the midbrain. These, you will remember, are subcortical visual and auditory centers. Finally, there is the *vestibulospinal tract*, which takes off from the nucleus of the vestibular nerve in the medulla. There are still other tracts from the brain to the spinal cord that we shall not name. You can see from this brief list, however, that the nervous system has a good many pathways for connecting up events in the brain with the motor neurons of the spinal cord.

The Final Common Path. The motor neurons of the spinal cord are a part of the various segmental and intersegmental arcs. But they are also a part of the much more complicated arc that includes ascending and descending pathways from the brain. Consequently the motor neurons do not belong exclusively to any one arc but serve as the final channel for many arcs. The somas of the motor neurons are "funnels" upon which many different impulses converge. It was for this reason that Sherrington many years ago called them "the final common path."

Just as a postscript to this point, we should mention another influence that bears on the final common path. This is kinesthesis. Kinesthetic fibers come back into the spinal cord from the muscles controlled by the motor neurons. They can "tell" the motor neurons what is happening in the muscles and thus guide or modify the activity of motor neurons. The kinesthetic impulses carry on this function even when the motor neurons are serving as the final common path for other spinal reflexes and for impulses from the brain to the spinal cord. Indeed, even the simplest reflex is usually guided by such kinesthetic impulses. The guidance may be a matter either of excitation or inhibition, but in many cases it is perfectly clear that the kinesthetic impulses inhibit. Thus they can restrain and smooth out the activity going on in motor neurons. We shall see some examples of this kind of influence later.

THE PYRAMIDAL MOTOR SYSTEM

We come now to the motor systems of the brain. These are interlinked in complex fashion and involve all the major divisions of the brain. Consequently there are many ways of talking about them. None is perfectly logical or simple. We have chosen an outline that we believe suits the present purpose. The major divisions of the outline represent three more or less distinct motor systems: (1) the pyramidal motor system, (2) the extrapyramidal system, and (3) the proprioceptor-cerebellar system. We shall talk about them in that order. Some other order might do just as well, but this one is convenient.

The Pyramidal Cortex. This part of the cortex is the beginning of a great motor pathway down to the brain stem and to the spinal cord. It is the origin of the *corticospinal* tract, which we mentioned in the previous section. It is also the beginning of some pathways that we will come to in a moment.

The pyramidal cortex gets its name from the shape of some cell bodies that are unique to it. These cell bodies are relatively large compared with those in the rest of the cerebral cortex, and they look like pyramids. These *pyramidal cells*, or Betz cells as they are called, are found only in the pyramidal cortex and only in layer V of that cortex (see page 48). It is the axons of these cells that make up the great descending motor pathways from the pyramidal cortex. We shall see, too, in a moment that these cells can be electrically stimulated to produce muscular contractions and movements in various parts of the body.

The pyramidal cortex also has other names. Sometimes it is called simply the motor cortex or motor area. Because the major part of the pyramidal cortex lies in the gyrus just in front of the central sulcus, it is sometimes referred to as the precentral gyrus or precentral area. Finally, in Brodmann's system of numbering areas of the cortex according to architectonic differences, area 4 makes up the larger part of the pyramidal cortex. We shall use these various names from time to time as they are appropriate.

ELECTRICAL STIMULATION

The motor functions of the pyramidal cortex were first established back in 1870 by the experiments of Fritsch and Hitzig. They applied electrical stimuli to the precentral gyrus and found that such stimuli caused discrete movements of the limbs and of various other parts of the body. In the many years that have followed, the method of electrical stimulation has been put to use in many studies to tell us how the motor cortex is arranged and what it does.

Somatotopic Organization. A most outstanding feature of the pyramidal cortex is that it is laid out in a very orderly fashion to represent different parts of the body (see Fig. 110). This arrangement is much like that of the somesthetic areas that lie just behind the pyramidal cortex in the postcentral gyrus. In animals that have a tail—Fig. 110 has been taken from the spider monkey just to illustrate this point—the extreme dorsal portion of the pyramidal cortex represents the tail. Electrical stimulation of this part will make the tail move. Then, taking the electrical stimulus to the more lateral parts of the pyramidal cortex, we find, in order, a leg area, a small trunk area, an arm area, and finally, in the extreme lateral and ventral sector, a face area. Stimulation of these sectors causes movements of corresponding parts of the body. Even the muscles for speech are included in this arrangement, for a stimulus applied to a certain part of the face area will produce vocalizations of one sort or another.

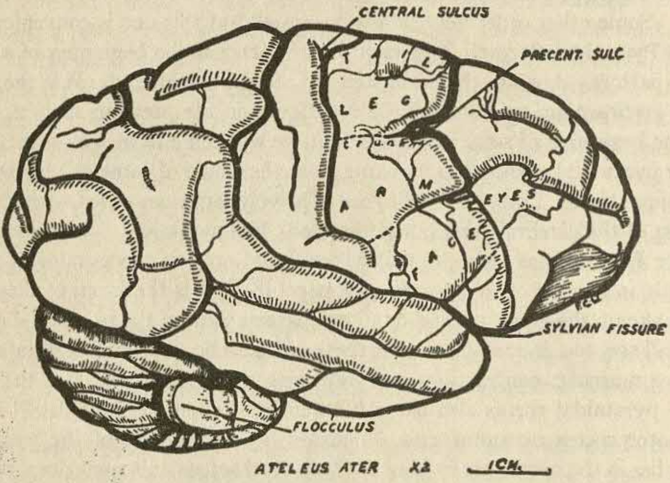

FIG. 110. Side view of the right hemisphere of the spider monkey showing the tail, leg, arm, and face representation in the motor area. (*From J. F. Fulton and J. G. Dusser de Barenne. The representation of the tail in the motor cortex of primates, with special reference to spider monkeys, p.* 408. *J. cell. comp. Physiol.*, 1933, 2, 399–426. *By permission of the Wistar Institute of Anatomy and Biology.*)

It is interesting to see how much space on the motor cortex is assigned to movements in different parts of the body. In Fig. 110 you can see that each part of the body does not get its fair share according to its size. Instead, space is assigned according to the skill and precision of movements controlled by the respective sectors. The *homunculus* of Fig. 111 illustrates this fact very well. The trunk, whose movements are large and crude, gets relatively little space. The legs get comparatively more, but the hands, which we use in refined skilled movements, get more than either the trunk or the legs. Then, when we come to the head, we see that the eyes, jaws, lips, tongue, and vocal cords get proportionately more space. This goes along with the fact that the eyes make extremely precise movements in fixating and pursuing visual objects and the lips, tongue, and vocal cords are involved in the very precise movements of speech.

This assignment of space in the pyramidal cortex preserves a relation that we have already seen in neuromuscular connections. Just as in the pyramidal cortex, the motor neurons of the spinal cord and brain stem are distributed to muscles, not according to their physical size, but according to their function in precise, skilled movements. You will remember that the innervation ratios for muscles of the trunk are different from those for the legs and eyes. There are many more muscle fibers of the trunk controlled by a central neuron than there are of the eyes. Thus the innervation ratios of motor neurons and muscle fibers reflect the same principle as the assignment of space in the pyramidal cortex.

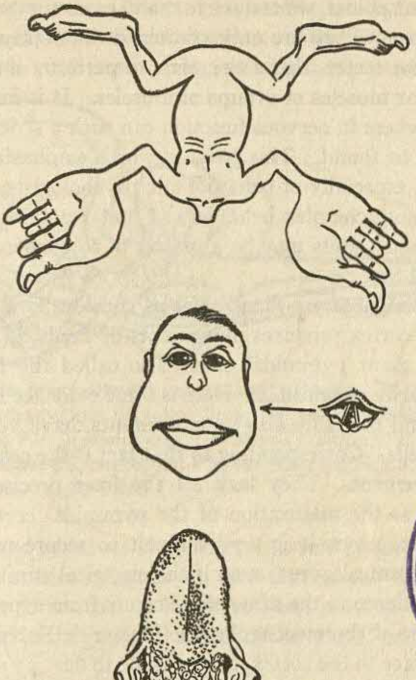

FIG. 111. A homunculus showing the relative extent and position of the representation of various parts of the body in the motor area of man. (*Based on the observations of Penfield and Boldrey*, 1937. *After Fulton.*)

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Movement Patterns. There is another important feature of the movements that are caused by electrical stimulation of the cortex. Briefly, it is that *move-*

ments, not muscles, are represented (see Hines). This statement holds just as much for the motor centers of the spinal cord as it does for the motor cortex. In exploring the motor cortex with an electrical stimulus, we can find different points that will give different movements. Yet if we compare the movements we get from different points, we can see in many cases that essentially the same muscles are involved. They are only combined differently. The assignment of space in the motor cortex, therefore, refers to patterns of movement and not strictly to particular muscles or groups of muscles. It is important to realize, moreover, that nowhere in nervous function can such a strict representation of particular muscles be found. This point is worth emphasizing in view of the frequent tendency, especially of behavioristic psychologists, to regard reflexes, and indeed even more complex behavior, as unit reactions. Considering behavior in terms of such units may be a matter of convenience, but it certainly is not one of actual fact.

Properties of Stimulability. Finally, let us consider how an electrical stimulus on the motor cortex produces movements of the body. All the evidence indicates that the giant pyramidal cells—also called the Betz cells—are the ones that are primarily responsible. Here is some evidence for that conclusion. Infant monkeys, and probably also human infants, have very poorly differentiated pyramidal cells. Corresponding to that fact is the coarseness and lack of skill in their movement. They lack all the finer precise movements that eventually appear as the maturation of the pyramidal cortex progresses. In infant monkeys, moreover, it is very difficult to secure motor responses by stimulating the precentral gyrus, even if the electrical stimulus is very intense (Hines). Other evidence to the same effect comes from experiments that make use of the technique of thermocoagulation (Dusser de Barenne). By applying a heated metal surface to the cortex, it is possible to destroy a certain number of layers—a number that depends on the temperature and the length of application of the coagulator. In these experiments, the pyramidal cortex remains excitable to electrical stimuli as long as the pyramidal cells are intact. When, however, the thermocoagulation goes deep enough to destroy the pyramidal cells, it is no longer possible to elicit movements by electrical stimulation of the cortex.

THE PYRAMIDAL TRACTS

These tracts make up the simplest and most direct of all motor pathways. They go directly to the motor neurons of the spinal cord and brain stem, which in turn serve the muscles. Sometimes, but not always, there are internuncial neurons between the axons of the pyramidal tract and the primary motor neurons (see Tower, Ranson).

As you might expect, there are two main divisions of the pyramidal tract. One is the *corticospinal tract*, which runs directly to the motor neuron of the spinal cord. It takes off from the leg, trunk, and arm areas of the pyramidal cortex. It is further subdivided, as we have already said, into a lateral corticospinal tract, which crosses over from one side to the other in the medulla, and a ventral corticospinal tract, which crosses in the spinal cord near the points where it ends in the ventral horn. The second chief division of the pyramidal tract is the *corticobulbar tract*. This serves the motor nuclei, located in the midbrain and hindbrain, of the cranial nerves that control movements of the eyes, face, lips, tongue, and vocal cords. As you might expect, this corticobulbar tract leaves the face and eye areas of the lateral surface of the pyramidal cortex. The pathway of the corticobulbar tract, like that of the corticospinal tract, crosses from one side to another in its course, but most of its crossing takes place in the brain stem in the general vicinity of the cranial nerves that it serves.

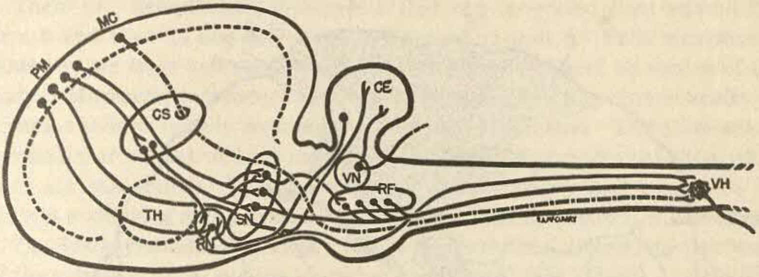


FIG. 112. Diagram of the principal motor centers and pathways. The dot-dash line represents the pyramidal pathway; the unbroken lines, the extrapyramidal pathways. *MC*, motor area of the cortex; *PM*, premotor area; *CS*, corpus striatum; *TH*, thalamus; *RN*, red nucleus; *SN*, substantia nigra; *CE*, cerebellum; *VN*, vestibular nuclei; *RF*, reticular formation; and *VH*, ventral horn cells. (*After Cobb.*)

THE EXTRAPYRAMIDAL MOTOR SYSTEM

As you can see, the pyramidal motor system is a rather simple one. Its center is an area of the cortex that is well defined. It is laid out to represent different parts of the body, and its pathways go directly to the motor neurons of the brain and spinal cord that control the muscles. A second system, the functions of which are interlinked with the pyramidal system, is the extrapyramidal motor system. This is by no means simple. It has so many centers and pathways connected in so many ways that it is difficult to understand them (see Fulton, Chap. 21).

In Fig. 112 you see a simplified diagram of the extrapyramidal system. It includes areas of the cerebral cortex, the corpus striatum lying just under the cortex, the red nucleus and the substantia nigra in the region of the midbrain, and some other centers in the hindbrain.

Areas of the Cortex. Several different areas of the cortex contribute to the extrapyramidal system. One area—the most important area—goes under several names: the premotor area, the intermediate precentral gyrus, and area 6 in the Brodmann system of numbering. Whatever it is called, it is the area that lies in the frontal lobe immediately in front of the pyramidal motor cortex of which we have just finished talking. This is the cortical area of greatest importance in the extrapyramidal system.

In addition to the premotor area, however, there are several other areas that contribute in one way or another to the system (see Fig. 113). Among them is an area that lies just in front of the premotor area and is sometimes called the "frontal eye field" or *area 8*. Another is *area 5*, which lies in the dorsal part of the parietal lobe just behind the postcentral somesthetic area. Still another cortical area contributing to the extrapyramidal system is *area 22* in the temporal lobe lying below and behind the lateral (Sylvian) fissure. There is, moreover, good evidence that area 3–1–2, which is primarily the somesthetic area (see page 266), and area 4, which we have seen as the primary pyramidal area, also make their contributions to the extrapyramidal system. So it is clear that there are quite a number of fibers drawn from many different areas of the cortex, some of them areas having other important functions, that contribute to the extrapyramidal pathways.

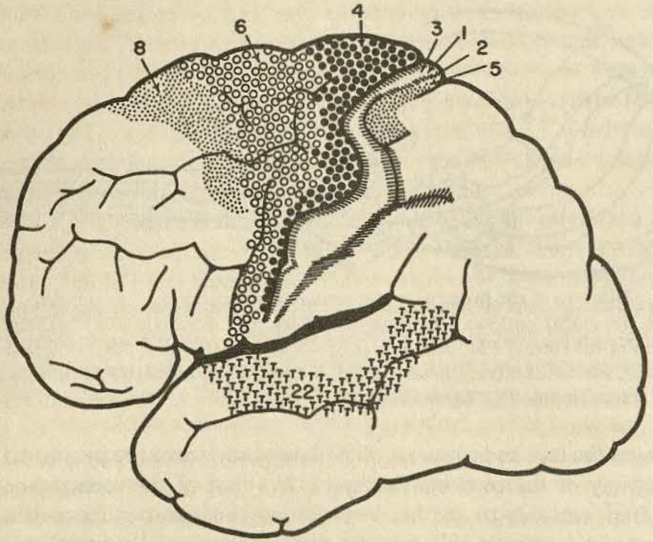


FIG. 113. Diagram of the areas of the human cerebral cortex involved in the extrapyramidal system. In the frontal lobe are areas 4, 6, and 8. In the postcentral region are area 3-1-2 and area 5. Down in the temporal lobe, area 22 is concerned in the extrapyramidal pathways.

Electrical Stimulation. Like the pyramidal cortex, the extrapyramidal areas are electrically stimulable (see Kennard). Movements of the body result when electrical stimuli are applied to them. There are, moreover, several important points to note about such movements. In the first place, when we get the movement by stimulating area 6, the premotor cortex, there is a fair chance that it is because current has spread to area 4, the pyramidal cortex. Thus some of the effects of stimulating the premotor extrapyramidal area are actually due to spread to the pyramidal area. To guard against this artifact in the experiment, it is necessary to remove the pyramidal cortex. If we do that, we may observe that stimulation of area 6 no longer produces any *specific* movements.

There are, nevertheless, movements that can be gotten from stimulating area 6 and that do not depend on any spread to area 4. Such movements, however, are large and stereotyped like turning of the head or torsion of the body. Moreover, to produce such movements requires a greater intensity of stimulus than is usually required by the pyramidal cortex. The other extrapyramidal areas that we have mentioned sometimes give movements, too, when they are stimulated. This, however, is not always the case. In some instances a stimulus only *facilitates*, but does not directly produce, a movement.

The Extrapyramidal Pathways. Unlike the pyramidal system, the pathways of the extrapyramidal system are rather complicated (see Fulton). In the first place, there are several relay nuclei on the way down from the cortex to the brain stem and spinal cord, and these nuclei have some very complex interrelations. In the second place, there is not just one pathway but several of them. That makes the pathways difficult to describe, but we shall do it very briefly and generally (see Fig. 112).

Corpus Striatum. The first 'stop' in extrapyramidal pathways is the corpus striatum, which lies below the cerebral cortex and above the thalamus. This is a very complex structure, made up of several nuclei that connect with one another in complex fashion. There is no need to go into its detail. We can simply note that fibers, principally from the premotor area, come down to it from the cerebral cortex and that fibers leave it to go on downward in the brain stem.

Substantia Nigra. The next stop in the extrapyramidal system is the *substantia nigra*. This is a complex nucleus lying in the brain stem in the region where the thalamus and midbrain join. It receives some fibers from the corpus striatum and also some directly from the cerebral cortex. From the substantia nigra there are fibers that course downward into the spinal cord to end on the somas of motor neurons in the ventral horn. There are other fibers that relay to another nucleus, the *reticular formation*, a complex structure of the hindbrain. Fibers from the reticular formation go, in turn, to the motor neurons of the spinal cord. Just to fill out an already complicated picture, we may note that the pathways from the substantia nigra and the reticular formation make up a tract called the *reticulospinal tract*, which can be identified in a cross section of the spinal cord.

Red Nuclei. Tracing the centers and pathways that we have just described, you will note that there is a corticospinal route for the extrapyramidal system just as there is for the pyramidal system (see Fig. 112). The difference is that there are several nuclei intervening in the extrapyramidal system. We have not, in fact, named them all yet. In Fig. 112 you will see another nucleus, the *red nucleus*, which we have not mentioned before. It, like the substantia nigra, lies in the region where the midbrain and thalamus join. It gets fibers from the premotor cortex in two ways, one directly and the other via the corpus striatum. In turn, it sends axons down through the brain stem into the spinal cord. These axons make up a tract known as the *rubrospinal tract*. So we have several tracts converging on the motor neurons of the spinal cord that come directly or indirectly from the cerebral cortex. The corticospinal tracts are the direct paths of the pyramidal system. The rubrospinal and reticulospinal tracts are indirect paths coming from nuclei that are relays in the extrapyramidal system.

The Corticopontocerebellar Pathways. Making up another main division of the extrapyramidal pathways are the fibers and nuclei of the corticopontocerebellar system. Fortunately, this pathway is not too complex. Axons come down from the cerebral cortex and end in the pons of the hindbrain. There are located the somas of neurons that send fibers into the cerebellum. That is all there is to the corticopontocerebellar pathway. It is of some importance in motor coordination.

THE PROPRIOCEPTIVE-CEREBELLAR SYSTEM

A third motor system for us to consider is the proprioceptor-cerebellar system. It is closely linked with the other systems we have been dealing with, but it is different enough and complex enough to be looked at as a separate system. The proprioceptor part of this system is, of course, sensory, but it is nevertheless part of this system for two reasons. First, the proprioceptors are the receptors that are primarily concerned with motor functions. There are two kinds of proprioceptors, the kinesthetic and the vestibular receptors. Both of them are stimulated only by the movements we make or the bodily positions that we assume. Thus the proprioceptors have much more to do with motor systems than with sensory experience. Secondly, and in a sense as a consequence of the first, the pathways of the proprioceptors lead rather directly to the centers and pathways of the motor system and particularly to the cerebellum. We have seen before, and we shall see again, that the kinesthetic pathways influence directly the motor neurons of the spinal cord as well as the motor neurons of the pyramidal cortex. Here in this section we shall also show you that proprioceptive pathways go directly to the cerebellum.

The Vestibular Receptors. In the earlier chapters on the senses we did not bother to consider the vestibular receptors. For that there were two reasons: (1) they do not enter very directly into sensory experience—we are not aware of their stimulation but only of their motor effects; (2) as we have just pointed out, they are primarily a part of the proprioceptive-cerebellar system. For that reason we shall describe them briefly here.

The nonauditory labyrinth is the name for the organ in which the vestibular receptors are housed. It consists of three principal parts: the *saccule*, *utricle*, and *semicircular* canals. They are all filled with a fluid—the endolymphatic fluid. We need not go into the details of their structure. The semicircular canals, however, function in one way and the saccule and utricle together in another way. They are all connected with one another by appropriate ducts. In each of the three semicircular canals there are enlargements called *ampullae*. These contain the sense organs of the canal, which are a group of specialized epithelial cells with hairs on them. These cells and hairs are embedded in a gelatinous mass (see Fig. 114), the *crista*, and they are served by fibers of the vestibular branch of the VIIIth cranial nerve. When a movement of the head causes endolymphatic fluid in the canals to move or to change in pressure, the crista is bent, and with the bending, the hairs that are embedded in it are stimulated. It is in this way that the vestibular receptors and fibers of the VIIIth nerve are excited.

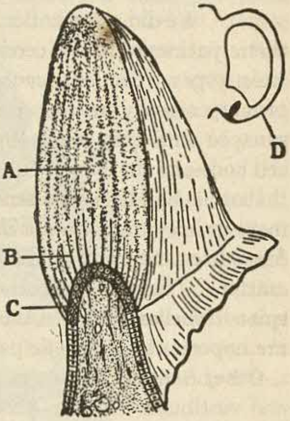


FIG. 114. Diagram of the crista and its position in the ampulla of the semicircular canal. *A*, gelatinous mass (cupula); *B*, hair tuft; *C*, hair cell; *D*, diagram of crista's position in ampulla of canal. (*After Schaffer. From E. G. Boring et al. Introduction to psychology. New York: Wiley, 1939. P. 622. By permission of the publishers.*)

The utricle and saccule work somewhat differently. They have groups of hairs, called *maculae*, located on their walls. They too are served by the VIIIth nerve fibers and, like the cristae, are stimulated by changes in pressure. The difference, however, between the maculae and cristae is this: the cristae are deflected only during a *change* of position of the head, in fact, only when the change is one of *acceleration* or *deceleration*, *i.e.*, when movement of the head is increasing or decreasing in speed. The maculae, on the other hand, are stimulated according to the resting position of the head. They are static, or *positional*, receptors.

The Vestibular Pathways. Like the neurons of the auditory branch of the VIIIth nerve, vestibular fibers have their cell bodies in the vicinity of the sense organs. The axons of these fibers join the auditory branch of the nerve just outside the bony labyrinth, and the two kinds of fibers, vestibular and auditory, run together in the VIIIth nerve toward the medulla. Just before reaching the medulla, however, the two parts divide again into vestibular and auditory branches. The majority of these fibers end upon cell bodies, making up the *vestibular nuclei* in the medulla. Some of the fibers, however, turn upward and go into the cerebellum without stopping. The vestibular nuclei are rather complex in structure and arrangement, but that makes no difference, for all they do is send their fibers into the cerebellum. Thus, with or without a synapse in the medulla, the pathway from the vestibular receptors ends up in the cerebellum.

The Kinesthetic Pathways. In dealing with the somatic sensory functions in an earlier chapter, we described the kinesthetic pathways to the thalamus and cortex. We did not mention the fact, however, that there are important kinesthetic pathways to the cerebellum (see Ranson). These pathways are of two main types. One is a *corticobulbocerebellar* route. In this, the axons of the primary sensory neurons enter the spinal cord and continue upward without synapse until they reach the cuneate and gracile nuclei in the medulla. The cell bodies in the nuclei, you will remember (see page 265), send fibers up to the thalamus, but they also send axons into the cerebellum. A second route is a more or less direct *spinocerebellar* pathway. In this case, however, some of the fibers from the primary sensory neurons end in the cord somewhere in the gray matter. There, second-order neurons send axons up the spinal cord in the spinocerebellar tracts to the cerebellum. Thus, in one way or another, there are important kinesthetic pathways to the cerebellum.

Other Sensory Pathways. We have known for a long time that kinesthetic and vestibular impulses make their way to the cerebellum. Their tracts were so obvious that we could not miss them. Only recently, however, has it been learned that the other senses also have their pathways to the cerebellum. This was found out by the method of evoked potentials (Snider and Stowell). Electrodes placed on the surface of the cerebellum give us electrical responses when the various senses are stimulated. In fact, there are very definite areas that can be mapped for vision, hearing, and the somatic senses. We do not know exactly why these sensory pathways to the cerebellum are there, but further research may tell us in due time.

The Cerebellar Cortex. The cerebellum is a very complex structure. In many ways it is just as complex as the cerebrum. In fact, from the evolutionary history of the cerebellum in vertebrate animals, it looks as though nature started out to make the cerebellum the highest center of the nervous system but then changed its mind and developed the cerebrum instead. At any rate, like the cerebrum, the cerebellum has a cortex of gray matter, and within that cortex there is white matter made up of fibers going to and leaving the cortex. Then, deep within the cerebellum, there are some subcortical nuclei. We shall come to each of these parts in turn.

There is no point in describing all the intricacies of the cerebellar cortex. To point out the general divisions and the connections that they make will be enough. Along the mid-line of the cerebellar cortex is an unpaired portion, called the *vermis* because it looks something like a worm. On each side of the vermis are a pair of lobes called the *cerebellar hemispheres*. For most purposes, however, there is no need to distinguish between the vermis and the hemispheres. A distinction that is more important to us is the division of the cerebellum into lobes which you can see in Fig. 115.

Different pathways end up in different lobes of the cerebellar cortex (not shown in Fig. 115). The vestibular pathways, coming from the vestibular nuclei of the medulla and to some extent directly from the vestibular nerve, end up in the ventral lobe of the cerebellum. Perhaps a few vestibular fibers get to other parts of the cortex, but in the main they go to the ventral lobe. The kinesthetic fibers, coming up the spinal cord in the spinocerebellar tract, go to the anterior and posterior lobes of the cerebellar cortex. Of these two lobes, probably the anterior lobe receives the greater proportion of spinocerebellar fibers. The fourth lobe, sometimes called the *middle lobe*, sometimes the *dorsal lobe*, is the end of the corticopontocerebellar tract—a tract that we met before in dealing with the extrapyramidal system. Thus the dorsal lobe of the cerebellum is, so to speak, under the control of the cerebral cortex.

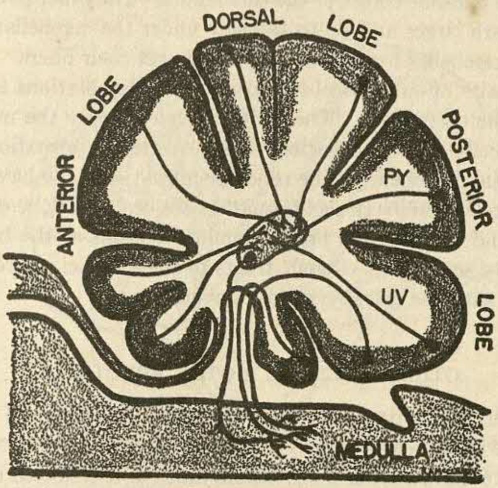


FIG. 115. Schematic diagram of a longitudinal section of the cerebellum. The cerebellum is divided into four main lobes: anterior, dorsal, posterior, and ventral. The two lower lobules make up the ventral lobe. The pyramis, *Py*, and the uvula, *Uv*, make up the posterior lobe. The shaded part in the center stands for the two groups of subcortical nuclei of the cerebellum, the dentate and fastigial nuclei.

That accounts in general for all the parts of the cerebellar cortex. Notice that all of it is sensory—at least, all of it receives fibers from sensory pathways or from the cerebral cortex. This is a rather different arrangement from what we find in the cerebral cortex.

Cerebellar Nuclei. If we now go on to see what fibers *leave* the cerebellar cortex, we run into another interesting arrangement (see Fulton, Krieg).

There are many fibers that we might call *motor fibers* leaving the cerebellar cortex, but few, if any, go out of the cerebellum. There are a few that go back from the cerebellar cortex to the vestibular nuclei of the medulla, but there are not many of them. Instead, all the so-called *motor fibers* from the cerebellar cortex go to the subcortical nuclei of the cerebellum and stop there.

There are two main subcortical nuclei. Each is found in pairs. One pair is the *fastigial nuclei*, which lie near the mid-line. They receive fibers from the vermis, *i.e.*, the mid-line cortex of the cerebellum. The other pair is the *dentate nuclei*. They are larger and lie to the side under the cerebellar hemispheres. It is from the cerebellar hemispheres that they get their fibers.

These two pairs of subcortical nuclei are the relay stations for getting impulses out of the cerebellum. The dentate nuclei supply the main tract, and this ends up chiefly in the red nucleus and the reticular formation. The tracts from the fastigial nuclei end in the reticular formation. We have already seen that the red nucleus and reticular formation are centers of the extrapyramidal system that send fibers to the primary motor neurons of the brain stem and spinal cord. By sending its efferent tracts to these nuclei, therefore, the cerebellum ties up with the extrapyramidal system.

OTHER CORTICAL MOTOR FUNCTIONS

You may feel by this time that you have had quite enough of the motor systems—they are indeed complex and confusing. Yet we have not told the whole story. We have quite a bit of information, much of it collected in recent years, about the motor functions of various areas of the cerebral cortex. We do not yet know what all of it means either for the physiologist or the psychologist, but we shall summarize it briefly, for in the years to come it should take on more and more meaning in understanding behavior.

Stimulable Areas

In talking about the pyramidal and extrapyramidal systems we have already noted that certain areas, particularly 4 and 6, of the cortex are electrically stimulable. Because we were then dealing with particular systems, we did not mention all the stimulable areas, nor did we make some important distinctions within the primary motor areas. That we shall do now.

Motor and Premotor Areas. Areas 4 and 6 in front of the central sulcus of the cerebral cortex have a finer degree of organization than we have admitted so far. Instead of only two areas, we can distinguish four different areas. For anatomical reasons that do not concern us, the nomenclature for these areas varies with the different primates. It is different in monkey, chimpanzee, and man. We shall follow the system for the chimpanzee, for that animal is most similar to man and has been thoroughly studied (McCulloch).

The four areas are 4*q*, 4*r*, 4*s* and 6. Area 4*q*, as you can see in Fig. 116, is the part of area 4 nearest the central sulcus. It is the most stimulable electrically of all the areas and gives motor responses to the weakest of stimuli. Area 4*r* lies in front of it (anteriorly). It is also stimulable but requires about twice as much energy as area 4*q*. The third area, 4*s*, is so named because it is a suppressor area—we shall see more of such areas in a moment—and was discovered only a few years ago. It looks as though it lies in area 6, but for a number of reasons it has come to be regarded as a part of area 4. Finally, area 6 is what is left of the intermediate precentral gyrus after we have accounted for the suppressor area 4*s*.

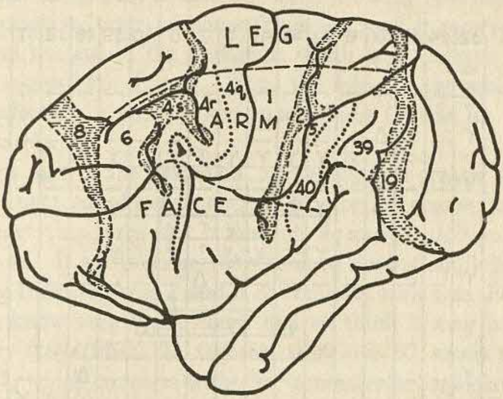


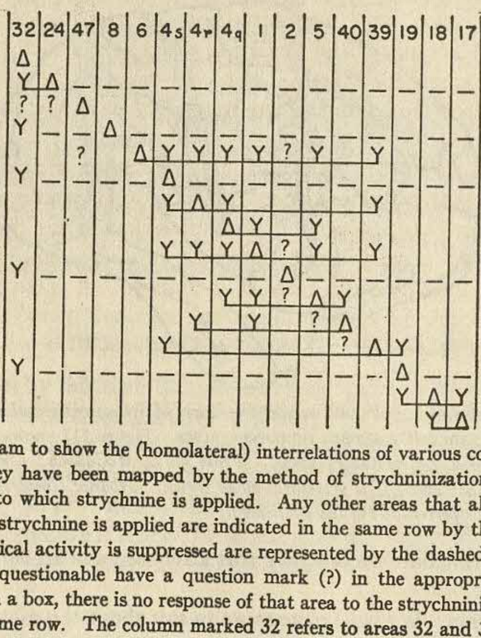
FIG. 116. The main excitatory and suppressor areas of the somatic and motor cortex of the chimpanzee. The shaded areas are suppressor areas. Figure 117 shows in detail how they are interrelated with the excitatory areas. (*From W. S. McCulloch. Cortico-cortical connections. In P. C. Bucy (Ed.), The precentral motor cortex. Urbana: University of Illinois Press, 1944. P. 233. By permission of the publishers.*)

The Eye Fields. We shall have more to say about the motor and premotor areas in a moment, but let us turn briefly to other areas with stimulable properties. These are the so-called frontal eye fields of area 8, lying just in front of area 6 (see Fig. 116), and the parietal eye fields of area 19, lying somewhat forward of the occipital visual areas. Stimulation of these areas has observable results in behavior. The frontal eye fields of area 8, when stimulated, give conjugate deviations of the eyes—the eyes move. At least a part of area 19, when stimulated, causes constriction of the pupils of the eyes.

In a moment we shall see other properties of these areas and how they are linked together. The important point to bear in mind is that we have six distinguishable areas or subareas of the cortex that produce some kind of behavior when they are stimulated: the primary motor area 4*q*, the secondary motor area 4*r*, the suppressor area 4*s*, the premotor area 6, the "frontal eye area" 8, and the parietal eye field 19.

CONNECTIONS BETWEEN CORTICAL AREAS

There are even more areas of the cortex that are concerned directly or indirectly in its motor functions. This we have learned through the application of a technique that has been extensively employed in recent years. It is the method of strychninization (see page 36), in which strychnine, a convulsive drug, is applied locally to a region of the cortex while electrodes placed in other areas pick up any resulting changes in activity. Strychnine always strongly excites or "fires" the region to which it is applied, and if some other area is affected by the use of the drug we know that there is a connection between the two areas. This technique of strychninization, used in conjunction with observations of changes in electrical activity of the cortex or of the behavior of an animal, has shown us how various cortical areas are interconnected in motor functions.



32	24	47	8	6	4_s	4_r	4_q	1	2	5	40	39	19	18	17
Δ															
Y	Δ	—	—	—	—	—	—	—	—	—	—	—	—	—	—
?	?	Δ													
Y	—	—	Δ	—	—	—	—	—	—	—	—	—	—	—	—
		?		Δ	Y	Y	Y	Y	?	Y		Y			
Y	—	—	—	—	Δ	—	—	—	—	—	—	—	—	—	—
					Y	Δ	Y					Y			
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					Y	Y	Y	Δ	?	Y		Y			
Y	—	—	—	—	—	—	—	—	Δ	—	—	—	—	—	—
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Y	—	—	—	—	—	—	—	—	—	—	—	—	Δ	—	—
													Y	Δ	Y
														Y	Δ

FIG. 117. A diagram to show the (homolateral) interrelations of various cortical areas of the chimpanzee as they have been mapped by the method of strychninization. Triangles (Δ) indicate the area to which strychnine is applied. Any other areas that also show electrical activity when the strychnine is applied are indicated in the same row by the open angle (Y). Areas whose electrical activity is suppressed are represented by the dashed line (—). Areas whose activity is questionable have a question mark (?) in the appropriate box. Where there is no mark in a box, there is no response of that area to the strychninization of the area indicated in the same row. The column marked 32 refers to areas 32 and 31, which respond together as a unit. (*Based on McCulloch*, 1944.)

Connections of Motor Areas. With the technique of strychninization, it has been possible to tell that certain areas of the cortex facilitate or even fire other areas concerned in motor function. All such interrelations between cortical areas have been summarized in Fig. 117. There a triangle (Δ) stands for the area to which strychnine was applied. *Y* stands for the area in which a discharge was seen. Where we are not yet absolutely certain that there is a connection, the doubt has been indicated by a question mark. Now let us consider briefly each of the areas in the illustration.

Area 4q. This area is the part of area 4 that is most stimulable electrically. You can see that it fires into no other part of area 4. On the other hand, this area has connections with two other cortical areas. One of them is area 1, the somesthetic area just behind the central sulcus. Firing in area 4*q* causes electrical activity in area 1. The physiologists who have done this work assure us that this means that there is an axon going from area 4*q* to area 1. Moreover, area 4*q* also sends fibers over to area 5. This, you may remember (see Chap. IV), is an "association" area for somesthesis—at least it receives fibers from the lateroventral nucleus of the thalamus, which is a thalamic relay station with the main somesthetic system. Thus the firing of the main motor area (4*q*) produces effects in a primary somesthetic area (1) and an "association" somesthetic area (5).

Area 4r. This part of the pyramidal area requires a greater stimulus than does 4*q* to evoke patterns of movement. It has cortical connections similar to, but more extensive than, area 4*q*. It fires into 4*q* and in addition fires into the suppressor area 4*s*. It sends connections back to the parietal lobe too, but instead of sending them to areas 1 and 5, it connects with area 39. This is an area we do not know very much about but we think it may be involved in complex memory (page 513). It, together with area 40, seems to be an outgrowth of area 7, which connects with the "somesthetic" association nuclei of the thalamus. At any rate, it has been regarded in clinical neurology as one of the parietal association areas of the cortex.

Area 6. The premotor area, the most important cortical center of the extrapyramidal system, not only sends impulses downward in this system but has extensive interconnections with other areas of the cortex. It discharges into all subareas of area 4—this is a one-way connection, for area 4 does not fire area 6—and also into sensory and association areas of the parietal cortex, *viz.*, areas 1, 5, and 39. Just what these extensive intercortical connections mean we do not know, but they must have some importance in the motor mechanisms of the brain.

Sensory Connections with Motor Areas. Not only do the motor and premotor areas fire other areas of the brain, but these other areas in turn have direct connections with the precentral areas. In Fig. 117 you can see that area 1, a part of the primary somesthetic cortex, fires back into the subareas of area 4. Area 5 in the parietal lobe, in addition to associating with sensory and "association" areas of the cortex, has connections with the primary motor area 4*q*. The two so-called association areas 39 and 40 (see page 48) also connect with some part of the precentral area, one with area 4*s* and the other with area 4*r*. So, in brief, there are ample intercortical links between the parietal sensory and association areas and the frontal motor regions.

Suppressor Areas. Now we come to another interesting aspect of intercortical motor functions. This is the existence, and the connections, of suppressor areas of the cortex. Such areas are called suppressor areas because, when they are fired with strychnine, they suppress rather than augment electrical activity in other areas of the brain. Sometimes the suppression is simply

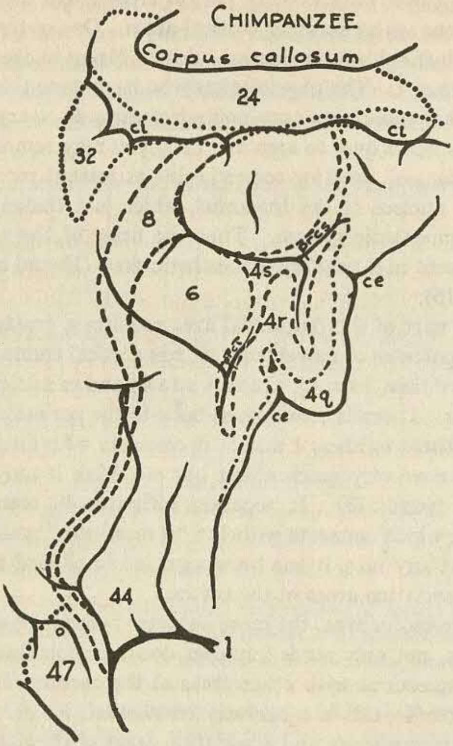

FIG. 118. The precentral motor cortex of the chimpanzee "unrolled." The top represents the cortical areas down in the longitudinal fissure above the corpus callosum. The middle represents the areas 4 and 6 normally seen on the dorsal surface. The lower part of the figure shows areas 44 and 47, located on the extreme lateral and orbital surface of the frontal lobe. The left part of the drawing is anterior; the right part is posterior. *Ci*, cingular sulcus; *Ce*, central sulcus; *prcs*, precentral sulcus; *prci*, intermediate precentral sulcus. (*Slightly modified from W. S. McCulloch. Cortico-cortical connections. In P. C. Bucy (Ed.), The precentral motor cortex. Urbana: University of Illinois Press,* 1944. *P.* 214. *By permission of the publishers.*)

of the spontaneous electrical activity that normally goes on in various areas of the brain (see page 548). Sometimes the suppression can be seen in behavior—it prevents or stops movements that otherwise can be elicited by stimulating one of the cortical motor areas.

To see the suppressor areas and where they are, we need to look at a new diagram of some of the cortical areas. Figure 118, unlike most illustrations of the brain, "unrolls" the cortex. It shows a large region of the cortex as though it were stretched out on a flat surface. At the top of the illustration are the parts of the cortex found down in the median longitudinal fissure—the medial cortex. The center of the illustration shows the dorsal and lateral surface of the cortex that is visible in the undissected brain. The lower part of the figure shows the part of the cortex on the extreme lateral and ventral surface that we can see ordinarily only by turning the brain upside down or dissecting some of it away.

This illustration shows some areas that have not been mentioned before. Area 24, for example, lies deep within the median sulcus above the corpus callosum. It makes up part of the cingular gyrus—of which more will be heard in the chapter on emotion—and lies below the cingular sulcus, which marks the end of the motor and premotor areas within the median sulcus. Areas 31 and 32, although separated somewhat from each other, function as one area, and they are connected by a strip along the cingular sulcus that separates area 24 from areas 4 and 6. On the lateral surface is area 44, which may be considered for the present purpose as part of area 6 and as functioning like area 6 (but see page 515). Area 47 lies in the inferior orbital surface of the frontal lobe ("down underneath"). We shall also meet this area later in Chap. XVII.

Area 4s. Altogether there are five suppressor areas that we know about so far (see Fig. 117). Area 4*s*, the strip between the motor and premotor areas, is one of them. This area, when it is strychninized, suppresses electrical activity in a large number of cortical areas. In addition to suppressing areas 4 and 6, it also suppresses practically all the sensory and "association" areas in the back of the brain, including the primary somesthetic and visual areas.

Area 8. It is interesting that area 8, the frontal eye field, is also a suppressor area. Indeed, it is much easier to see its suppressor activities than any of its stimulable properties. Only after rather lengthy stimulation will it evoke eye movements, but it immediately suppresses patterns of movement as well as electrical activity in different areas when it is stimulated. This area suppresses practically all the areas of the brain.

Area 2. This area is a strip running along in the hind part of the postcentral somesthetic area. It seems to have somesthetic sensory functions. Nevertheless, when it is stimulated it does a good job of suppressing activity in practically every other sensory and motor area of the cortex. For the specific areas suppressed, see Fig. 117.

Area 19. This is supposed to be part of the cortical visual system. It is called the parastriate area and has some visual functions. But it is a suppressor area, too. In Fig. 117 you can see that its activity does just as thorough a job of suppressing response in other cortical areas as do any of the suppressor areas.

Area 24. This area, deep in the central sulcus, plays a unique role. It has no motor functions that we know of, nor any sensory functions either. As we shall learn later, it is probably connected in some wav with emotion. Despite that fact, it is a suppressor area for many motor and sensory centers of the cortex. In fact, in Fig. 117 you can see that its excitation suppresses activity in the same list of centers as do most of the other suppressor areas.

Area 31–32. As we indicated above, areas 31 and 32 ought to be considered as one area. They lie in the median sulcus between the cingular gyrus (area 24) and the motor and premotor areas. They are not suppressor areas. They nevertheless have a unique role in the suppressor system. They are excited by the activity of suppressor areas. In Fig. 117 you can see that whenever any of the suppressor areas (2, 4*s*, 8, 19, or 24) are fired, areas 31–32 also fire. Just what this means we do not know, but it is a consistent fact.

Area 47. This is not a suppressor area, either. We do not know exactly what it is, although later we shall see that it seems to have an important role in general bodily activity. The significant thing about it here is that it gets suppressed. Whenever any of the suppressor areas are firing, area 47 gets suppressed along with many other areas of the cortex.

COMMENT

That ends the brief review of the cortical interrelations of the motor systems. There are many details concerning the routes of these interconnections and the relations between the two sides of the brain that we have left out. This outline, however, gives the main points.

In two of the chapters that follow there will be some rather scanty information about the role of some of these areas in behavior. We should make no pretense, however, of understanding the meaning of these extensive relations between the different cortical areas. Our main reason for including this section is to show what the possibilities are for interconnections between the motor and sensory systems. Another reason is that research is proceeding apace in this general field, and it may be only a few years before the facts take on important meaning. When they do, the reader may be somewhat better prepared.

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CHAPTER XIV

REFLEXES

The concept of the reflex goes back to Descartes in the seventeenth century. He was writing and thinking long before we knew about nervous impulses. To him, the stimuli of the world about us, as well as the events going on in the nervous system, were all the work of animal spirits. He thought of animal spirits entering our bodies through the sense organs, flowing into the nervous system through the nerve "tubules" and out again through the tubules to the muscles, finally making the muscles contract. Thus he thought that we sometimes perform automatic acts because the nervous system reflected animal spirits coming in through our sense organs to the muscles. Today we know that the events in the reflex arc are releases of energy, not the flow of animal spirits, but the concept of the reflex remains the same. Reflexes are more or less automatic movements that come about because the nervous system "switches" incoming sensory impulses into outflowing motor paths.

Phasic and Postural Reflexes. Most of the time, when we think of reflexes, we have in mind some specific movement. We think of the leg jerking when the knee is tapped or the eyelid winking when a light is flashed. Such brief, specific movements, however, make up only one of the major classes of reflexes. They are the *phasic reflexes*. There is also a second main class, which is more important but not quite so obvious, the *postural reflexes*. These are always at work in any normal animal or human being. They are longer lasting, sustained reactions. They keep our head up and our trunk erect without our thinking about it or intending to do anything. In this chapter, in which we shall summarize what we know about reflexes, we shall take up both kinds of reflexes, the phasic and the postural.

Classes of Reflexes. There are many reflexes, and we must have some way of classifying them in order to deal with them. One way—the way that is most convenient—is to use different levels of the nervous system for our classification. That gives us three main classes of reflexes: segmental, intersegmental, and suprasegmental reflexes. The rest of the chapter falls into these three categories, and we shall explain them as we come to them.

SEGMENTAL REFLEXES

The first two classes of reflexes just named, the segmental and intersegmental reflexes, are spinal reflexes. They occur entirely at the spinal level. In the first class, the segmental reflexes, are included only those reflexes that depend upon one segment of the spinal cord. In such reflexes, the nervous impulses that enter the spinal cord from the somatic end organs pass out over the motor axons of the same segment or level. Intersegmental reflexes, on the other hand, are those that in one way or another involve several segments of the spinal cord. The sensory impulses that set off the reflex come into the cord at different segments from those going out over the motor pathways to the muscles concerned.

THE NATURE OF THE REFLEX

Before we take up different kinds of segmental reflexes, we ought to think for a moment about what the reflex is. A segmental reflex is the simplest kind of behavior to be seen in any organism. Yet it is a highly organized affair. It is a pattern of response that is made up of many neuromuscular units, all acting together with precision of timing and of amount of contraction. The pattern is not simply a mechanical contraction of a particular group of fibers but rather a pattern of movement. As one of our leading neurophysiologists has said, "The simplest spinal reflex 'thinks,' so to say, in movements, not in muscles." (See Fulton, page 51.) In saying this he does not mean that there is anything mystical about the reflex, but only that the reflex is a functional pattern, not merely "a cog in a machine."

Reciprocal Inhibition. There are always several factors at work in making the particular pattern of movement in a reflex. Some of them were mentioned in an earlier chapter (IV). One of these factors is *reciprocal inhibition.* This is inhibition of a motor neuron by kinesthetic impulses coming back into the cord from the muscle that the neuron serves or from other muscles closely allied to it. In lifting a leg, for example, there are two sets of antagonistic muscles involved. One set, the flexor muscles, must contract, and another set, the extensor muscles, must partly relax, if the leg is to lift. Otherwise there may be a conflict between the antagonistic muscles and nothing may happen. In the simplest flexion reflex, therefore, there must be a smooth coordination of the contraction of the flexor muscles and the relaxation of the extensor muscles. This coordination is achieved by each set of muscles sending into the spinal cord kinesthetic impulses that inhibit or regulate the motor neuron serving the other set of muscles. In this way a smooth pattern of movement results in the flexion reflex.

Recruitment and After-discharge. There are two other important factors that affect the pattern of movement in a reflex. One is *recruitment*—getting more and more internuncial neurons of the spinal cord to bring impulses to bear on the motor neurons. Back in Chap. IV we saw how it is possible for sensory neurons bombarding internuncial neurons with impulses gradually to bring more and more internuncial neurons into play. The end result of this mechanism of recruitment is to make a reflex build up smoothly and gradually rather than in a jerky, mechanical fashion. A second factor is *after-discharge.* This refers to the impulses that continue to bombard the motor neurons after sensory stimulation has stopped. We know it to be due at least in part to the arrangement of internuncial neurons in circuits so that impulses, once started by sensory stimulation, can reverberate in the circuits for some time afterwards (page 75). The role of after-discharge in simple segmental reflexes is to make a response disappear slowly and smoothly rather than abruptly.

Other Factors. Besides these specific factors affecting the pattern of the reflex, other parts of the nervous system are always influencing a reflex. Even though the entire pathway for a segmental reflex may be within a segment of the cord, there is no escaping the ever-present bombardment from other pathways and levels of the nervous system. The motor neurons of any one segment receive internuncial neurons from sensory fibers at other levels of the cord, and these internuncials are usually bringing in impulses that affect the segmental reflex. In the last chapter, moreover, we saw that the various pathways of the pyramidal and extrapyramidal systems from the brain—the corticospinal, reticulospinal, and rubrospinal tracts, to mention only three—make connections with the motor neurons at all segmental levels. Some of these influences are inhibitory, some are excitatory, but they are nevertheless influences, and they modify what happens in a segmental reflex.

You probably can see now why we said that a reflex is a pattern of movement, not a mere mechanical contraction of muscles. The most elementary reflex response in a normal animal or human being takes place in a milieu of events converging on it from many parts of the nervous system. One must look at the reflex as a 'figure' on the 'background,' and the form that the 'figure' takes depends on the 'background' of other stimuli and responses occurring at the same time.

Experimental Methods. All this has its point not only for understanding the nature of the reflex but also for the methods that physiologists use in studying the reflex. In order to see spinal reflexes in their simplest form and to free them as much as possible from 'outside' influences, physiologists observe a number of precautions in their experiments. For one thing, they usually cut all nerves to muscles other than the ones they wish to study. In this way they get rid of some of the intersegmental influences on segmental reflexes. As another precaution, they usually keep the general posture of an experimental animal as constant as possible by placing the animal in a comfortable rack that gives it support. Finally, to get rid of the influence of the pyramidal and extrapyramidal pathways coming from the brain, they usually study spinal preparations, *i.e.*, they cut the spinal cord at some point between the brain and the segments they wish to study.

TYPES OF SEGMENTAL REFLEXES

Now we may take up briefly some of the more important segmental reflexes. First of all, we should note that there are two general classes of reflexes, the *flexion* and *extension* reflexes.

Flexion Reflexes. A flexion reflex is any response of a leg or arm in which part or all of the limb bends toward the body and away from the ground. In the main, a flexion reflex is a phasic response, although in certain special cases it may be a sustained postural response. The reflex is one of the most primitive of the phasic reactions because it occurs in response to any painful stimulus and is the means by which an animal avoids or escapes such a stimulus.

There are many variations in the pattern of the flexion reflex and there are many factors that affect it. The flexion may take place at the ankle, the hip, or the knee, or it may involve all these joints in varying degrees. How much flexion occurs depends in part on the kind of sensory stimulus that produces it and in part on its intensity. Painful stimuli bring forth the greatest flexion reflexes—those that involve the ankle, knee, and hip—as do also very intense stimuli. Pressure stimuli sometimes call forth flexion reflexes, but usually somewhat smaller ones, for as we shall see, pressure is also the stimulus for some antagonistic extension reflexes.

Also affecting the vigor and pattern of the flexion reflex are the impulses that come down from the brain to the segmental levels. When these are eliminated, by cutting the descending motor pathways, larger and more complete flexion reflexes are obtained than when part or all of the brain is allowed to send its impulses to the reflex center. Apparently the motor impulses from the brain tend to 'inhibit' the flexion response, partly perhaps by direct inhibition and partly by helping extension reflexes that inhibit the flexion reflex through reciprocal inhibition (see page 303).

Myotatic Reflexes. The other general class of segmental reflexes is the *extension reflexes.* There are several types of such reflexes. One is called the *stretch reflex* or, sometimes, the *myotatic reflex.* This is an increased tension or contraction in extensor muscles. Such muscles support the animal's body against the pull of gravity and for this reason are sometimes called the antigravity muscles. These muscles have in them two types of receptors—the annulospiral and flower-spray (see page 256)—which are stimulated whenever the muscles are stretched. Just as a matter of simple mechanics, the muscles are stretched whenever their antagonists, the flexor muscles, contract, but the stretching stimulus calls forth the myotatic reflex, which makes the extensor muscles contract. Thus the myotatic reflex is really a circular reflex. Stretching the muscle sets up impulses that go into the spinal cord and out again to contract the muscle.

You can see that the myotatic, or stretch, reflex is a fine balancing mechanism. As such, it can work as both a phasic and a postural mechanism. The phasic reflex occurs when an extensor muscle is suddenly stretched, and the result is a quick increase of tension in the muscle. The myotatic reflex is also a postural reflex, however, because it maintains a constant *tonus*, or a slight tension, in an extensor muscle even when the limb is not being flexed. Put another way, any tendency of the muscle to stretch sends some impulses back the reflex pathway to keep it slightly contracted.

The myotatic reflex, whether phasic or postural, is usually limited to the muscle in which stretching (the stimulus) occurred. Sometimes, however, it may include other extensor muscles of the same limb that are related in function to the muscle stretched. This reflex, as we shall see later, is a basic reaction in many aspects of behavior.

It is worth pointing out in passing how the myotatic reflex ties in with the difference between red and white muscles. In the last chapter we explained that red muscles contain food stores that suit them to sustained postural activity, whereas white muscles can work only for brief periods of time. As we have just seen, myotatic reflexes make up a sustained postural mechanism, and it is interesting that the muscles that participate in myotatic reflexes always have a good proportion of red fibers in them. Flexor muscles and other muscles that do not give myotatic reflexes usually have only white fibers in them. The facts concerning the capabilities of red and white muscle and those concerning the myotatic reflexes in posture therefore all tie together.

Extensor Thrust. There is another type of extension reflex, the *extensor thrust*, which is worth a moment's thought. This is a reaction of a limb in which the limb straightens out to support the body against gravity or to thrust the body into the air. The stimulus that produces an extensor thrust is any pressure on the pads of the foot or, in animals like the dog or cat, a quick separation of the toe and foot pads. The extensor thrust is one of the reflexes that enable us to walk or run, for it comes into play to support the body whenever the foot touches the ground.

Crossed Extension Reactions. Closely related to the extensor thrust is another type of extension reflex, the *crossed extension reaction*, which also helps out in walking and running. This reaction is an extension of the leg opposite to the leg that is stimulated to flex. It comes into play more slowly than does the extensor thrust, and it is slower both in reaching its peak and in relaxing. The timing of this reaction is quite important, for it counteracts the flexion reflex in the limb that is raised from the ground and it prepares this limb for extension at the same time that the other limb is on the ground and supporting the body.

INTERSEGMENTAL REFLEXES

As we have already explained, reflexes whose pathways involve more than one segment of the spinal cord are called intersegmental reflexes. There are two general classes of intersegmental reflexes, the *somatic* and the *autonomic*, which correspond to two general divisions of the nervous system. We have already indicated the general pathway for autonomic reflexes in Chap. III, and we shall deal with such reflexes again in connection with emotion (Chap. XVI). Here, therefore, we shall deal only with the somatic intersegmental reactions.

In general, when we use the term intersegmental reflex, we do not imply any essentially new type of response. Instead, we refer to a composite or pattern of segmental reactions that occurs because several stimuli are present at the same time or in quick succession at different segmental levels of the spinal cord. Thus the term intersegmental reflex does not, in general, indicate responses fundamentally different from segmental reflexes, but it refers rather to a different level of neural organization.

Cooperative Reflexes. Intersegmental patterns sometimes involve the cooperation and sometimes the competition of the more elementary reflexes that make them up. Thus we can think of two types of intersegmental patterns, the cooperative and competitive reflexes. In cooperative reflexes, two or more reflexes mutually aid each other or follow each other in a smooth pattern. In competitive reflexes, the pattern that we see comes about because two or more incompatible reflexes are instigated by different stimuli acting at the same time.

A good example of a cooperative reflex is the *scratch reflex*. This is a repetitive rhythmic movement of a limb, and analyzed into its parts, it is the alternation of two reflexes, a flexor and an extensor reflex. It has its rhythmic pattern because, by reciprocal inhibition, a flexor reflex first suppresses an extension response and then the resulting stretching of extensor muscles sets up an extension reflex in which the flexion is suppressed. So on it goes in alternation. It is the peculiar quality of the stimulus, moreover, that makes the two components cooperate in the scratch reflex. The stimulus for the reflex is 'bright' pressure on two nearby points of the skin, either at the same time or one right after the other. Put another way, it is 'itching' or 'tickling' stimulus that calls forth the scratch reflex. In an earlier chapter on the skin senses, we saw that this kind of stimulus arouses both the pain and pressure pathways. Pain impulses, we have just seen in an earlier chapter, tend to call forth flexion responses and pressure impulses the extension reflexes. When these two stimuli are combined, the result is not a conflict of reflexes but rather a rhythmic cooperation of the two that serves a very good purpose—especially if there happen to be any fleas around.

The Final Common Path. We have already taken up the notion of the final common path. So far, however, we have applied it only to the primary motor neurons of the nerves that go out to striated muscles. These neurons are the final common path for all behavior because nothing can happen in the striated muscles without impulses passing through these neurons (see Fig. 119).

For certain purposes, however, other neurons may become part of the final common path. For example, as we shall see in the next chapter, the pyramidal neurons from the motor cortex down to the primary neurons are part of the final common path for 'voluntary' coordinated behavior. More to the point, however—and the reason for bringing the matter up here—is the fact that *internuncial neurons* may become part of the final common path for competitive intersegmental responses. In such responses, the internuncial neurons take on the properties of a final common path because reciprocal inhibition is at work (see page 78). In this kind of inhibition, internuncial neurons are used as 'switches'—they determine which of two competing reflexes will have the right of way. Whichever way the internuncial neuron goes, so goes the reflex. It is good to have this notion in mind as we consider the competitive reflexes.

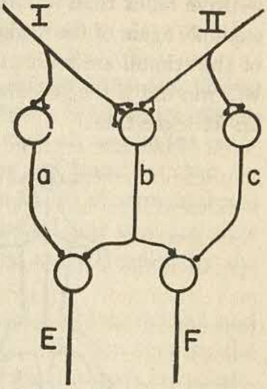

FIG. 119. Diagram illustrating reciprocal inhibition and the final common path. Neuron *b* in the center is the critical neuron. Impulses come to it from two or more other neurons, I and II, and it serves as the final common path for them. When neuron *b* is an internuncial, it may serve as the 'switch' in reciprocal inhibition. Neurons *E* and *F* must have two or more impulses arriving simultaneously on their somas to fire. If neuron *b* synchronizes with neuron *a*, then *E* fires. If *b* synchronizes with *c*, then *F* fires. (*After Gasser*, 1937.)

Competitive Reflexes. These reactions are cases of the competition of two or more sensory stimuli for the final common path. When there is such competition, one of several things may happen: (1) one stimulus may take over the final common path to evoke one of the two possible reflexes and to inhibit the other one; (2) exactly the reverse may happen; or (3) the final common path may be taken over first by one stimulus and then by the other so that the two stimuli take turns at calling forth their respective reflexes.

Of these several possibilities, there are several factors that may decide which of them happens: In the first place, the nervous system is so constructed that certain types of reflexes tend to win out over other reflexes. If, for example, stimuli are present for bringing forth both the flexion reflex and the scratch reflex, the flexion reflex will usually win out. Nature apparently gave the flexion reflex this priority because, of all the reflexes, it most quickly and surely avoids harm. For this reason too, flexion reflexes also tend to win over extension reactions. An animal or a human being, for example, that is wounded in the foot often will fall on the ground because the painful stimulus brings out flexion reactions and inhibits the extensor reactions needed for standing up.

A second factor deciding which of two competing reflexes occurs is the relative intensity of their respective stimuli. Other things being equal, the stronger stimulus will call out its reflex and suppress the reaction to the competing stimulus. In the case of the flexion reflex vs. the scratch reflex, for example, the flexion reflex will lose its priority in favor of the scratch reflex if the 'itch' stimulus for the scratch reflex is relatively strong and the painful stimulus for the flexion reflex is relatively weak.

A third factor that can decide the competition between reflexes is timing. If a reflex has been going on for some time, it is more likely to lose out to a competitive reflex than if both reflexes were started at the same time. To use the example again of the flexion vs. the scratch reflex, even if the relative intensities of the stimuli are such as to give the scratch reflex priority, the flexion reflex will win out if the stimulus for it comes after the scratch reflex has been going on for some time.

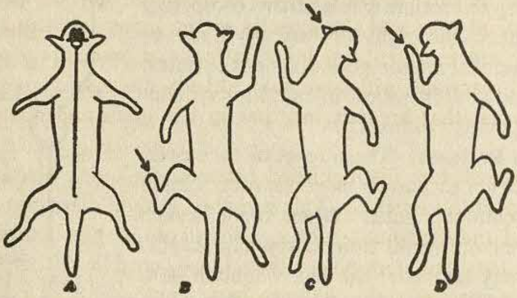

FIG. 120. The reflex figure. *A*, resting position after decerebration; *B*, *C*, and *D*, positions taken following stimulation of the part of the body indicated by the arrow. (*After Sherrington. From C. H. Best and N. B. Taylor. The physiological basis of medical practice. Baltimore: Williams & Wilkins,* 1939. *P.* 1317. *By permission of the publishers.*)

Successive Induction. These are the general principles of competition between reflexes, and there is no need to go into a lot of detail. There is one particular phenomenon, however, that is worth a little attention because it shows us how we manage to walk and move around. The phenomenon is *successive induction.* It is the outcome of competition among reflexes, in which antagonistic reflexes follow each other in a definite pattern. If, for example, a pressure stimulus is applied to the bottom of the foot, it tends to call forth the antagonistic reactions of flexion and extension. Suppose, however, that for some reason or other the flexion reflex temporarily dominates and the leg lifts. Then an extension reaction will tend to follow. One reason for this sequence is the factor that we mentioned above—once the flexion reflex has had its turn, it tends to give way to the antagonistic extension reflex. Another factor, of course, is that the flexion stretches the extensor muscle and initiates a myotatic reflex reaction of the extensors. The net result is the successive induction of two reflexes in a pattern of flexion and extension.

The Reflex Figure. The principle of successive induction also works to produce more complex patterns of reflexes. One such pattern is the reflex figure, which is basic to walking and running. You can see it illustrated in Fig. 120. The pattern involves interaction of reflexes in all four limbs. A flexion reflex in one hind limb causes a crossed extension reaction in the opposite hind limb. The flexion reflex of a hind limb is also accompanied by an extension of the forelimb on the same side. The result is a precise alternation of steps in the limbs that we all use—animals and human beings alike—in walking.

SUPRASEGMENTAL REFLEXES

Now we shall move on to study the reflexes that depend upon the centers and pathways of the brain—the suprasegmental reflexes. None of the reflexes of this type can be carried on by the brain alone, for they all require the pathways of the spinal cord and the muscles of the limbs and trunk for their expression. The suprasegmental reflexes, in fact, are made up of segmental and intersegmental reactions, which we have already discussed, but they are more complex patterns, that are put together in the brain and controlled by the brain.

We have twice before distinguished between the quick phasic reflexes and the sustained postural reflexes. This is a good general distinction between the suprasegmental and the spinal reflexes. Not all of the spinal reflexes are phasic, but in general they are more phasic than those controlled at the higher levels. Even the extension reactions that are basic components of our postural reactions tend to be phasic when controlled only at the spinal level. It is when the extensor reactions are controlled and organized into patterns by the action of the higher centers that they make up true postural mechanisms. As a general principle, then, the suprasegmental centers organize reflexes into postural patterns.

Decerebrate Rigidity

This principle has a striking illustration in a phenomenon that has come to be called decerebrate rigidity. Such rigidity is pictured in Fig. 121. It is a complex postural pattern, but its main feature is the contraction of all the extensor, or antigravity, muscles of the arms and legs as well as other muscles of the body that normally contract with them (Sherrington). Sometimes, therefore, decerebrate rigidity is also called extensor rigidity. It is a general and basic postural pattern, and for that reason physiologists have spent a great deal of effort on finding out the centers and pathways whose activities cause it. The main outlines of the story are now clear.

Definitions. To tell it, we must go back and inquire about the methods and consequences of decerebrating animals. Strictly speaking, a decerebrate animal is one in which the cerebral hemispheres have been cut away from the rest of the nervous system. In such animals, moreover, we see signs of the extensor rigidity that we have just described. In common practice, however, decerebrations are often done at lower levels in the brain and with a better display of extensor rigidity. An animal may be decerebrated by cutting away all

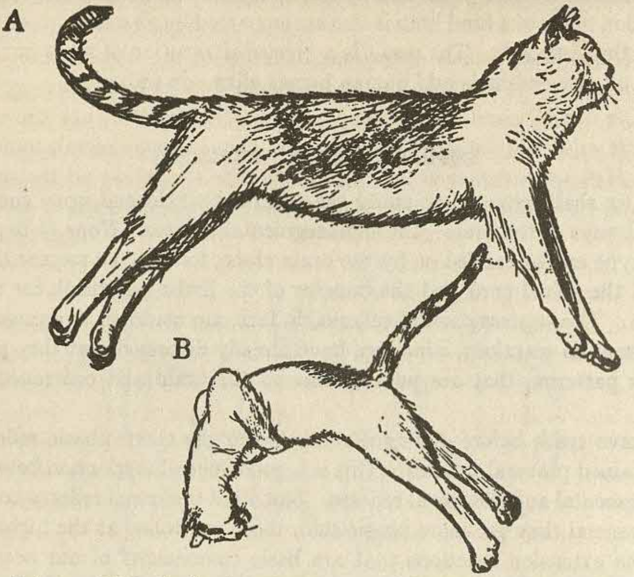

FIG. 121. Extensor rigidity in the decerebrate cat. *A*, decerebrate with intact labyrinths; *B*, decerebrate and labyrinthectomized. (*After Pollack and Davis. From C. H. Best and N. B. Taylor. The physiological basis of medical practice. Baltimore: Williams & Wilkins, 1939. P. 1338. By permission of the publishers.*)

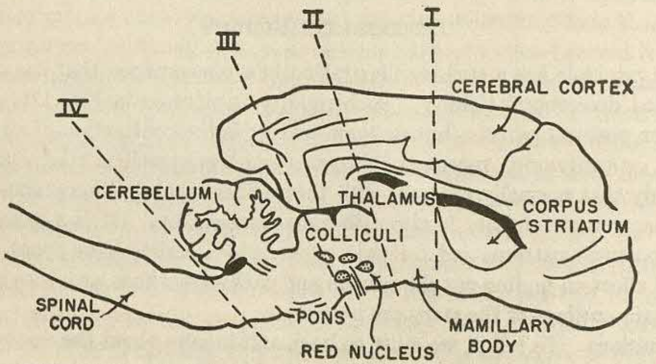

FIG. 122. Diagram of levels of decerebration in experiments on decerebrate rigidity in the cat. I, a very high decerebration that cuts out only the front part of the cerebral cortex and the corpus striatum; II, a somewhat lower decerebration that cuts out a great deal of cerebral cortex, the thalamus, mammillary bodies, and corpus striatum; III, a low decerebration that cuts off the colliculi, midbrain, red nucleus, and all higher centers; IV, very low decerebration that severs almost the whole brain except for some parts of the medulla. (*After Best and Taylor*, 1940.)

the brain above the thalamus, above the midbrain, or even above the medulla.

We describe these various operations in terms of the highest level of the brain left intact. For example, the *bulbar* animal has its brain stem sectioned between the medulla and the midbrain, the *midbrain* animal has the section between the midbrain and the thalamus, and the *thalamic* animal, sometimes called the *high decerebrate*, has the cut between the thalamus and the cerebral hemispheres. In some of the experiments that have been done to study extensor rigidity only the cerebral cortex has been removed; in others only the cerebellum has been taken out. In these cases we speak, respectively, of *decorticate* and *decerebellate* preparations.

Factors in Rigidity. From all the experiments that physiologists have done, we now know that there are three factors in the production and control of extensor rigidity. These are the extrapyramidal system, the kinesthetic pathways, and the vestibular pathways. Of these three factors, the vestibular influences are the primary cause of the extensor rigidity. The extrapyramidal and kinesthetic influences, on the other hand, inhibit or modify the rigidity produced by vestibular impulses. Altogether, the three factors make a balanced system for the control of extensor posture. Here, in brief, are some of the facts to support these statements.

Extrapyramidal Inhibition. First of all, it is the interruption of the extrapyramidal system that causes extensor rigidity to develop in the decerebrate animal. This fact is proved by experiments, illustrated in Fig. 122, in which decerebrations have been done at various levels of the brain and on either one side or both sides of the brain.

If a cat is decerebrated *on only one side* at the level of the midbrain, an extensor rigidity develops on that side. Because the pyramidal motor system crosses below the level of the midbrain, this system cannot be held responsible for the rigidity. The extrapyramidal system, on the other hand, is a good suspect, for it is not a crossed system.

The suspicion is confirmed when we learn that the amount of extensor rigidity that develops is proportional to the amount of the extrapyramidal system that is removed. High decerebration, which takes out only the striate and cortical portions of the system, produces only slight effects. With lower decerebrations the symptoms are more prominent and persistent. The extensor rigidity becomes particularly severe when the decerebration is low enough to cut out the *red nucleus*—a nucleus that we know to be a principal center and relay station of the extrapyramidal system. We may therefore conclude that the red nucleus is of special importance in inhibiting extensor rigidity. In other experiments, however, taking out the red nucleus by itself does not produce the rigidity. It is fair to conclude, therefore, that it is the additive effects of the parts of the complex extrapyramidal system that inhibit extensor rigidity.

Along the same line, we might add that taking out the cerebellum—which contributes to the extrapyramidal system by sending fibers to the red nucleus and reticular formation—enhances any extensor rigidity that may have been produced by decerebration.

Kinesthetic Inhibition. The combined effects of the centers and pathways of the extrapyramidal system are clearly the most important factors in inhibiting extensor rigidity. Experiments tell us, however, that kinesthetic influences can and do add their share of inhibition. One can, for example, electrically stimulate some of the muscles of the limbs, thereby contracting them. The kinesthetic impulses that arise from this contraction will inhibit the extensor tonus of the opposite limb in a decerebrate animal. Then, too, if one stimulates a sensory nerve, thus sending in kinesthetic and cutaneous impulses to the spinal cord, the extensor tonus of decerebrate rigidity will be inhibited. So also will electrical stimulation of the dorsal kinesthetic column of the spinal cord. In these cases extensor tonus gives way to the reflex figure described above. These, briefly, are some of the ways of showing that kinesthetic factors, as well as extrapyramidal influences, control and inhibit extensor tonus.

Vestibular Excitation. The third factor in extensor rigidity—the factor that is primarily the cause of it—is vestibular. There are several ways of arriving at that conclusion. For one thing, we do not see extensor rigidity in the spinal animal, and that means that the cause of the rigidity must reside at a level above the spinal cord. In the bulbar animal, on the other hand, extensor rigidity is more severe than in animals decerebrated at any higher levels. That means that the cause of the rigidity must lie in the medulla. Its locus has been narrowed down further by making sections at different levels in the medulla. These experiments tell us that so long as the section is above the vestibular nuclei we get extensor rigidity, but when the section is below the nuclei we do not. The vestibular nuclei, therefore, are the source of the extensor rigidity.

When the whole story is put together, this is the picture we get. The vestibular pathways continually pour impulses into the nervous system that, by themselves, would produce the general extensor posture that we call extensor rigidity. These impulses are modified and inhibited by the general activity of the extrapyramidal motor system. Moreover, in the case of specific parts of the body and specific reflexes, they are also inhibited by kinesthetic stimuli coming in from muscles at the same general segmental level of the body.

PLASTICITY OF BEHAVIOR

We have told the story of extensor rigidity and may now turn to some of the other suprasegmental reflexes. Closely related to extensor rigidity are some other reactions that we see in the decerebrate preparations, the *lengthening* and *shortening* reactions (Sherrington). Taken together, these reactions make up what we might call *plastic* reactions because they allow the positions of limbs to be molded much as one might mold some plastic or clay.

The lengthening and shortening reactions are illustrated in Fig. 123. The base line of the figure represents a limb that is partly flexed to make an angle of about 60 deg. at the knee. The lines moving away from the base line indicate greater and greater flexion up to an angle of about 110 deg. We can see the shortening reaction when the limb is being flexed and the lengthening reaction when it is extended. In either case, the terms "shortening" and "lengthening" refer to what is happening in the extensor muscles of the limb.

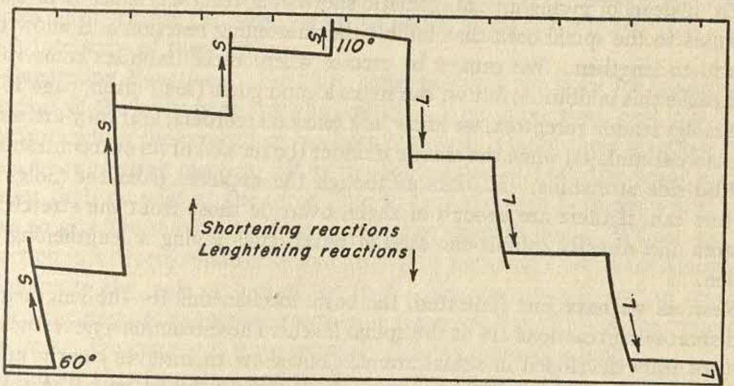

FIG. 123. Shortening and lengthening reactions. The diagram is from an experiment with a leg muscle of a decerebrate cat. At bottom left, the leg makes an angle of 60 deg. Each *S* marks a shortening reaction when the leg is passively flexed. Lengthening reactions are indicated in the right-hand part of the figure. (*From C. S. Sherrington. On plastic tonus and proprioceptive reflexes, p.* 118. *Quart. J. exp. Physiol.,* 1909, 2, 109–156. *By permission of the publishers.*)

Shortening Reactions. This is a tendency for an extensor muscle to shorten either actively or passively. There are two ways to demonstrate the tendency in decerebrate animals. (1) When one passively *flexes* a limb, he will encounter some resistance. The leg does not 'want' to flex. This is due to a reflex contraction of the extensor muscles that counteracts flexion. (2) If, on the other hand, an experimenter passively *extends* a limb, there is no special resistance, and the leg easily assumes the new position to which it has been extended. In this case, the extensor muscles shorten with the passive extension. A series of shortening reactions are pictured in Fig. 123. Such shortening reactions, we can say with assurance, are manifestations of *stretch reflexes*. They come about because passive flexion of the leg slightly stretches the extensor muscles, and this stretching sends back impulses from the stretch receptors that reflexly cause the extensor muscles to shorten.

Lengthening Reaction. Superficially, the lengthening reaction appears to be just the reverse of the shortening reaction, but it involves a different mechanism. If in the same situation we have been talking about, we attempt to flex a leg forcibly, we first encounter resistance because the shortening reaction is keeping the extensor muscles partly contracted. If we continue the flexion rapidly, however, the resistance suddenly "melts" away and the leg can very easily be set in a new flexed position. The "melting away" of resistance in the face of forced flexion is called the lengthening reaction.

What happens in this reaction is that when the extensor gets stretched too much, instead of giving an antagonistic shortening reaction, it sends in some impulses to the spinal cord that inhibit the shortening reaction and allow the muscle to lengthen. We cannot be certain where these impulses come from that cause this inhibition, but we can make a good guess (see Fulton, page 152). The Golgi tendon receptors, we know, are tension recorders, and they are often intensely stimulated when the muscle is under the tension of its own contraction and outside stretching. It looks as though the impulses from the Golgi receptors can, if there are enough of them, override those from the stretch receptors and directly inhibit the stretch reflex, thus giving a lengthening reaction.

Now, as we have just indicated, the basic mechanisms for the lengthening and shortening reactions are at the spinal level. These reactions, nevertheless, are not fully developed in spinal animals but show themselves clearly in decerebrate preparations. They are, therefore, closely linked with the suprasegmental mechanisms of extensor rigidity. They are brought into play both because of some stimulating influence, perhaps vestibular, and because some of the motor pathways, perhaps both the pyramidal and extrapyramidal pathways, which normally inhibit the reactions, are removed by decerebration.

We have said that these lengthening and shortening reactions make an animal plastic, for they allow us to mold its limbs in almost any position we want. It is important to realize that this plasticity of behavior is something we see, not only in decerebrate animals, but also, under certain circumstances, in "normal" animals and human beings. Patients sometimes display it when they have tumors that may do to them about the same thing that partial decerebration would. More important, however, is the fact that animals or human beings with no known damage to their brains may also show this plastic behavior. Sometimes people suffering from a psychosis called *catatonic schizophrenia* show it, and we also often see it in the after-stages of epileptic fits, when there is unconsciousness, coma, and the same sort of waxy plasticity. We simply mention the phenomena at this point, but this is not the place to go into them in detail (see Chap. XXV).

THE POSTURAL REFLEXES

The extensor reactions that we have been talking about make up only one of the general aspects of posture. Several other phenomena of posture form a class of reflexes known as the *postural reflexes.* Some of them are little more than changes in tonus in certain parts of the body, but others are rather complex movements. Indeed, one can grade postural reflexes on a scale ranging from the most general tonic reactions, such as extensor rigidity, to more specific and complex adjustments. In general, the higher the status on such a scale, the more does an adjustment depend on the higher brain centers. Extensor tonus, the more basic and general postural mechanism, is organized, as we have just seen, at the level of the medulla. Some of the more specific postural reflexes, however, are tied together at the higher levels of the brain. Let us now look into some of these reflexes.

Supporting Reactions. First are some postural reactions for maintaining support of the body in an upright position. We can see them best in a dog or cat from which the cerebellum has been removed. One of these reactions is the *positive supporting reaction.* It is the contraction of both the flexor and extensor limb muscles at the same time so that the limb becomes a stiff pillar able to give the maximum of support to the animal's body. We can get this reaction in a decerebellate or bulbar animal by applying a tactual or kinesthetic stimulus to the pads or toes of the foot. Just the opposite sort of reaction, called the *negative supporting reaction*, is the relaxation of all of the muscles of the limb. We can see it if we passively flex the digits of a limb.

Without these negative and positive supporting reactions, neither man nor animals could walk. When we shift the weight of our bodies onto one leg, that leg becomes stiff because of the positive supporting reaction. Meanwhile, the other leg without our weight on it relaxes because of the negative supporting reaction, and flexion reflexes come into play to take our steps for us. Thus the supporting reactions are important in the normal animal. Moreover, they are made up of component flexion and extension reflexes that work at a purely spinal level. The fact, however, that we can see them best in an animal without its cerebellum or decerebrated above the medulla shows us that they are primarily organized in the hindbrain and are then subject to the influence of higher centers.

Shifting Reactions. Quite akin to the supporting reactions is the so-called shifting reaction. A brief example will tell what this reaction is. If an experimenter passively flexes the left hind limb of a dog and at the same time causes the animal's body to veer toward the left, a strong extensor tonus develops in the flexed limb. This is the shifting reaction. Its 'purpose' presumably is to support the body under the new conditions of shifted weight. We can see this sort of response almost any day in an animal when we push the animal's body from one side to the other or forward or backward. The response is due, we know, to kinesthetic impulses from the limb muscles *stretched* or extended when the body veers. Experiments with this reaction in decerebrate animals have made it clear that the reaction is primarily organized in the medulla, for we can see it in bulbar animals. The reaction, however, is somewhat more dependable and precise in the midbrain animal than it is in the bulbar animal. This tells us that the midbrain helps out the medulla in organizing the reaction.

Tonic Neck Reflexes. There is another group of reflexes, which involve the muscles of the body more or less as a whole. They have been called the *tonic*, or *attitudinal*, reflexes because we see them in an animal when it is putting itself in readiness for some complex response. These reflexes are called forth by kinesthetic impulses from the neck muscles, from vestibular impulses, or by a combination of the two. Because there have been experiments to separate the effects of these two kinds of stimulation, we can subdivide the tonic reflexes into two classes according to the kind of stimuli that produce them. The *tonic neck reflexes* have been studied in animals whose vestibular receptors have been destroyed, and conversely the *tonic labyrinthine reflexes* have been observed in animals whose kinesthetic pathways have been interrupted. Thus we can take up separately these two kinds of tonic reflexes.

There are several *tonic neck reflexes*, not just one. We can see them in a number of different situations. (1) When the head of an animal is rotated, extensor tonus increases immediately in the limbs and trunk of the side of the body toward which the jaw is turned. At the same time the extensors of the limbs on the other side of the body—the side toward which the top of the head is turned—relax. This is one example of a tonic neck reflex. (2) Another is the case of turning the head toward one shoulder. Because of the kinesthetic impulses that arise in the neck, extensor tonus increases in the limbs of the side toward which the head is turned and decreases in the limbs of the opposite side. (3) Still another case is the bending of the head upward. This increases extensor tonus in the forelimbs and decreases it in the hind limbs—a posture that we can see in a normal animal when it is looking upward. Conversely, when the head is bent downward, extension in the forelimbs decreases and that in the hind limbs increases.

All these reactions have been called "attitudinal" adjustments because they are the changes in our posture that we need to make when we get ready to do something. Take the example of the cat.

> When a cat standing on all fours hears a noise ahead and to its right, its head turns and the extremities on the right side automatically exhibit increased extensor posture, which would tend to support the weight of the body in case the animal takes off with its left forelimb. If the noise is made by a mouse, the cat has only to decide whether to dash at it or not—the postural adjustments for the act are made automatically.[1]

Tonic Labyrinthine Reflexes. In order to study the second class of tonic, or attitudinal, reflexes, the tonic labyrinthine reflexes, we need only to get rid of kinesthetic influences. That is done easily enough by cutting the dorsal spinal roots, for it is through these roots that kinesthetic impulses from the neck come into the nervous system. The reactions that we then observe can be set off only by the vestibular receptors, and from experiments of this kind we learn that there are definite vestibular reflexes to changes of the position of the head. For example, when the head is pointed 45 deg. upward above the horizontal plane, high tonus develops in the extensor muscles. Conversely, when the head is pushed downward at an angle of about 45 deg., extensor tonus greatly decreases. With the head in intermediate positions, of course, extensor tonus is also only moderate.

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[1] Fulton, p. 168.

Changes in posture due to vestibular stimulation by the position of the head are exactly what we would expect. They correspond to the adjustments either we or animals make when we prepare to rise from a reclining to a standing position. Other experiments tell us, too, that these reflexes are *positional,* not movement, responses. They depend upon the utricle and saccule of the labyrinth, for which position is the stimulus, not upon the semicircular canals, for which acceleration or deceleration is the stimulus.

In the experiments we have been talking about, physiologists have deliberately separated the kinesthetic and vestibular influences so that they could tell what each contributes to the tonic or attitudinal reflexes. In the normal animal, however, there is undoubtedly an interaction between the reactions from the two kinds of stimuli. For the labyrinthine reflexes include contraction in the neck muscles, and these contractions afford kinesthetic stimuli which may in turn bring about tonic neck reflexes. Thus the vestibular receptors can bring about tonic reflexes both directly and indirectly through the kinesthetic stimulation resulting from the primary labyrinthine reactions.

Righting Reactions. There is a family of reflexes, called the *righting reactions*, that help an animal or human being to regain its balance when, for some reason, it has been thrown off balance. Different sensory stimuli can set off the reactions, and different parts of the body can take part in them. These differences can be used for classifying the righting reactions, and altogether five main classes have been distinguished. We shall describe them very briefly, saying just enough to tell what they are and what stimuli evoke them.

Labyrinthine Righting Reflex. The stimulus for this reflex, as its name implies, is a change of position of the vestibular organs. In this reflex, whenever the head is turned away from the normal position, the reflex brings the head back whether or not the body is in a normal position.

Body-righting Reflex Acting upon the Head. When an animal is laid on its side, there is a strong tendency for it to turn its head into the normal horizontal position. This has been called the *body-righting reflex acting upon the head* because it is a reaction to the asymmetrical stimulation of the body. The tactual and kinesthetic receptors stimulated on one side, because the animal is lying on its side, are the receptors whose stimulation calls out the reflex turning of the head.

Neck-righting Reflex Acting upon the Body. The two reflexes that we just mentioned bring an animal's head into the normal horizontal position with respect to the ground. When such reflexes have been called out and yet the body is left in an abnormal position, there is tension in the muscles of the neck, more on one side than on the other, depending on which way the body is twisted. The tension in the muscles of the neck on one side arouses kinesthetic impulses, and these start off a chain of postural responses in which first the arms, then the trunk, then the hindquarters are rotated into the horizontal position. In other words, in this reflex the body rights itself because the head has already been righted and the resulting tension in the neck muscles calls forth the body-righting reaction.

Body-righting Reflex Acting upon the Body. This is similar in principle to the reaction we have just described. This reflex occurs when an animal is placed in a lateral position and force is applied to the head or shoulders. Then the whole body tends to right, with the hindquarters starting off the reaction.

Optic-righting Reflexes. As their name implies, these are reactions to visual cues in which the head and body are turned into an upright position. The animal or human being making the reaction looks at objects in visual space and uses these as visual cues to get himself righted.

Neural Centers. There have been a lot of experiments to find out what centers and pathways underlie the righting reflexes. We have known for some time now that the visual area of the cortex must be present for the optic-righting reflexes to take place. The optic-righting reflex is, in fact, the only reflex of all those we have talked about so far that is organized at a cortical level. There has been some trouble, however, in identifying the centers for the other righting reflexes. For some time it looked as though the thalamus and midbrain were necessary for these reactions and particularly as though the red nucleus of the extrapyramidal system were the center most important in organizing them. This does not seem to be true. At least, one can completely destroy the red nucleus without doing any great harm to the righting reaction. There is a good deal of evidence, however, pointing to the general region of the red nucleus and to the reticular formation as the place in which the righting reactions (except the optic reaction) are organized. There has been a great deal of research on this problem, and the meaning of some of it is in dispute, so we cannot be too positive about it. It is fair to say here only that all the nonvisual righting reactions are organized somewhere in the hindbrain, and we must let it go at that.

Cortical Postural Reflexes

We are coming now to the last of the suprasegmental reflexes. You have seen that the basic components of these reactions take place in the pathways of the spinal cord but that the brain organizes them and puts them together in many different patterns. Within the brain, too, you have seen that there are successive levels of organization. The hindbrain and the centers within it are primarily responsible for organizing most of the reactions that we have dealt with, but in many cases the midbrain and forebrain help out and add something to the events going on at the lower levels. So far, you have seen only one example of a reflex organized at the cortical level—the optic-righting reflex. Now, as we approach the end of the chapter, there are three other reactions, all of which depend on the cerebral cortex, that we ought to take up.

The Grasping Reflex. This reflex is easily seen in babies and infant monkeys and also in primate animals in which certain parts or all of the cerebral cortex is gone. It is a strong flexion of the fingers when some object touches the palm of the hand. The stimulus is tactual, and ordinarily, if it is not too large, it is grasped firmly by the fingers. Sometimes this reflex is so powerful that it can support the weight of the entire body for a considerable length of time. It is present in most human infants at birth, but it grows less pronounced with age and tends to disappear after five or six months (see Richter). Even infants, who are not capable of doing much else, can sometimes support their bodies by reflexly grasping a finger or a stick.

Looked at superficially, the grasp reflex appears to be a flexion reflex. It is, in fact, a flexion of the fingers. On every other score, however, it should be classed as an extension reflex. In the first place, it is used for supporting the body, as are the extension reflexes. In the second place, we see it in various experiments under the same conditions in which extensor tonus and extension reflexes are very prominent. In fact, we would have mentioned it earlier along with extensor rigidity and extensor reactions, had it not been for the fact that the grasp reflex is controlled by higher centers of the brain than most of the extensor reactions. And in the third place, it is connected with the same motor system of the brain, as we shall see, as some of the extensor reactions.

That brings us to the question of what centers of the brain are responsible for it. There are a good many studies of the question, and here are some of the points that they bring out. The grasp reflex, we now know, is like extensor rigidity in that it appears because lower centers are free from the control of higher ones (Richter and Hines). Extensor rigidity, however, occurs because centers in the medulla are free from the inhibiting influences of all the higher centers of the extrapyramidal motor system. The grasp reflex, on the other hand, appears because centers—probably higher in the brain than the medulla, but we do not know—are freed from *cortical* influences.

These influences, we know, are primarily in the premotor areas of the extrapyramidal system, for after bilateral removal of the premotor areas, grasping appears in full force. These areas, however, are not the only ones of importance, because forced grasping gradually disappears in animals with only the premotor areas removed. The pyramidal area of the cortex is somehow involved too, for it is only when physiologists take out both the premotor and the motor areas that the grasping reflex appears and stays for good. What the pyramidal cortex has to do with the grasping reflex, we do not really know. Perhaps it is the extrapyramidal pathway from the motor cortex that makes the difference, or perhaps the pyramidal pathways cooperate with the extrapyramidal system in suppressing the grasp reflex. It will take further research to straighten us out on this point.

Placing and Hopping Reactions. The last two types of reactions for us to take up are closely linked. They are the placing and hopping reactions. Both depend for their existence upon the integrity of certain areas of the cerebral cortex. Both are adjustments of the limbs in such a way as to bring about better support for the body.

Placing Reactions. Placing reactions may arise from either visual or somesthetic stimuli. In the visual reaction, an animal that is being held in the air with its legs hanging free will attempt to place its legs on any solid object near by in the field of vision—so long as the eyes are not blindfolded and the visual cortex is intact (Smith).

There are, on the other hand, several kinds of somesthetic placing reactions (Bard). When an animal is held with the edge of a table in contact with the back of its feet, the legs will be put on the table. So will they, too, when the animal's chin or vibrissae touch the table. Also, when an animal is standing on the edge of a table and then is suddenly pushed forward so that its forelimbs hang over the edge, the animal will lift its legs backward to regain its previous position. Whenever, finally, the leg of an animal is passively lifted and then released, the leg will at once be lowered back to the table for the 'purpose' of being used again to support the body. That, very briefly and rapidly, is a description of the different kinds of placing reactions.

Hopping Reactions. The hopping reaction is a complex reaction, consisting first of a flexion of the leg, then a lateral movement, and finally an extension, all in quick succession—much as a person behaves when he has been shoved off balance. The reaction is easy to get in an animal (*e.g.*, a monkey) that has been made to stand on one leg and then, by a push, is made to veer forward, backward, or sideways. The animal will make a series of hops that serve the purpose of getting the limb squarely beneath him again for support. Such hopping reactions have been studied in the rat, cat, and monkey.

Cortical Basis. Both hopping and placing reactions depend upon particular areas of the cortex (Bard and Brooks). In the rat, in whose cortex it is usually difficult to find any localization of function, the reactions are abolished when a rather large but definite dorsal area of the cortex is taken out on both sides. In the cat, the reactions are 'localized' somewhat more precisely in areas analagous to the motor areas of higher animals. And in monkeys, the functions of hopping and placing are confined to the precentral and postcentral cortical areas.

Each of these areas is essential. Without the motor abilities localized in the precentral (pyramidal) area, the hopping and placing reactions are lost. So are they too, when the primary somesthetic (postcentral) areas are removed. So it appears that in the higher primates both the somesthetic areas and the primary motor areas are essential to the hopping and placing reactions. The visual placing reactions that depend upon the visual cortex are, of course, an exception to this statement.

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CHAPTER XV

COORDINATION

As we have said before, there is no sharp line to draw between different types of motor functions. From a behavioral point of view, there are only different emphases and levels of description. From the physiological point of view, there are different levels of organization of behavior patterns. So this chapter will not deal with behavior that is qualitatively different from that which we took up in the last chapter. Instead, we shall study merely more highly organized patterns of behavior. We shall also deal with some of the basic problems of understanding coordinated patterns of behavior.

What we take up will fall into three main categories. (1) We shall see how behavior patterns develop and how the physiological mechanisms that underlie them arise. (2) We shall consider the mechanisms of the brain that account for the skill and coordination of our voluntary movements. (3) We shall look into some special problems of recovery of function—how the brain manages to compensate for damages in our motor mechanisms.

THE DEVELOPMENT OF BEHAVIOR PATTERNS

If we want to know how something works, we often can learn a good deal by seeing how it is put together. So it is with the mechanisms of behavior. We can understand the physiological motor mechanisms by studying their development, both in the evolutionary series and in the growth of particular individuals. Here, therefore, we shall run over rather briefly some of the things we know about the development of behavior patterns and motor coordination in phylogeny and ontogeny.

PHYLOGENETIC DEVELOPMENT

Speaking very generally, it is possible to divide most patterns of behavior into two categories, *locomotor* and *manipulative* behavior. In locomotion the animal moves itself about in its environment. In manipulation an animal stays still and moves objects in its environment. Most of the reflexes and postural reactions that we talked about in the last chapter can be combined in one way or another to fit into this general distinction.

Locomotor Behavior. The distinction is useful because it helps us get a general picture of how behavior patterns have changed in the phyletic series.

Fishes, as we all know, have no arms or legs, although they do have fins for appendages. They have almost no manipulative abilities—unless gulping food is manipulation—but they are locomotor animals. By patterns of contracting their segmented body muscles they swim about in the water, sometimes with great speed and skill. In fishes, the most lowly members of the vertebrate series, we therefore see well-developed locomotor abilities but no manipulative skills.

In further evolution, nature has provided for different, and sometimes more effective, modes of locomotion. Amphibia, which form a bridge between the fishes and the higher vertebrates, develop appendages for locomotion. They use these appendages for getting about when they get to the point in their life span when they leave the water and come to live on land. We see these appendages, two arms and two legs, in almost all the higher vertebrates. Only in a few forms, like the snake and the whale, has nature "slipped back" to the original form in fishes and left off, wholly or partly, the appendages. In all the other four-legged animals, locomotion is more or less highly developed. In the birds, two of the limbs, the arms, are modified into wings for locomotion in the air, while the hind limbs move the animal about on the ground. There are other minor modifications of the structures and patterns of locomotion, but the general picture of four-legged locomotion remains the same throughout vertebrate evolution.

Manipulative Behavior. The important change in patterns of behavior comes late in evolution. It is the development of manipulative ability, and it occurs in the mammalian series. If we think of manipulation in broad terms, we can note three different kinds of manipulative patterns—those having to do with the hands, the mouth, and the eyes. These patterns tend to evolve together in evolution, but they are worth distinguishing.

The Hands. Skill in manipulating the hands and fingers steadily increases in the mammalian series. It is particularly prominent in the monkeys, apes, and man. Rats or rabbits show a little such skill, but not much. They use their "hands" somewhat to hold food that they are eating. Occasionally, but not often, they may use them to pull a string or manipulate some object. In general, however, we see only the rudiments of manual skill in the rodents. In dogs and cats we see more of it. These animals use their paws to push objects around, in play, and sometimes even for signaling purposes. Monkeys, of course, do a lot with their hands, using them for grooming, for support, for carrying food to their mouths, and for handling objects. The chimpanzee can handle sticks and rakes to use them essentially as tools. And man's great abilities with his hands are so well known that we do not need to describe them. The trend toward increasing manual skill in mammalian evolution is unmistakable.

The Eyes. Not quite so obvious but equally important are similar trends in other types of manipulative ability. Consider the eyes. Lower animals, such as birds, do not move their eyes very much independently of the head. They usually move their heads when they want to look from one object to another. The same is true of the lower mammals, such as the rat and guinea pig. Cats and dogs, however, show some fairly definite movements of the eyes without the head. In monkeys and man the trend becomes very definite; these higher animals are capable of a fine degree of coordination of the eyes. You can see this best perhaps in the great skill required for a man to read the lines of print in a book.

The Mouth. The story is much the same with mouth movements. In animals like the rat, cat, and dog we see the mouth used a little as a means of manipulating the environment. Objects are picked up, held, and carried about in the mouth. In some of the lower animals, too, we see the mouth and vocal cords used to make a few sounds that can serve as signals. Only in the primates and man, however, has there been a great improvement in 'vocomotor' ability. Indeed, although we may not realize it, the skill of motor coordination of the lips, tongue, and vocal cords that is required for human speech is the most delicate and highly elaborated of all man's motor abilities. Manipulating sounds and words is a skill that is almost solely man's special ability and surpasses the other skills that he has acquired.

Cortical Evolution. There are remarkable changes in the nervous system that go along with the status of locomotion and manipulation in evolution. Although locomotor abilities change very little in the later stages of the phylogenetic series, there is a change in how the nervous system takes care of locomotion. In the mammals, locomotor patterns come to depend more and more on the cerebral cortex. In a dog or cat, for example, taking out the entire cerebral cortex, although it has some serious results, does not interfere very much with the locomotor abilities. Decorticate cats and dogs can stand and walk. In the monkeys and man, however, locomotion depends much more on the cortex. Without the cortex they cannot stand or walk. So, in brief, the mechanisms that control and integrate locomotor patterns are transferred to the cerebral cortex in the later stages of mammalian evolution.

But even more striking is the way in which the cerebral cortex grows and enlarges with the development of manipulative behavior. Unlike locomotor patterns, such behavior is not first organized at a subcortical level and then transferred to the cortex. Its very appearance in evolution goes along with its dependence on the cortex. Back in Fig. 116, you can see just how much of the cortex is involved in manipulative behavior. The motor and premotor areas that we have already met with before, the frontal eye fields (area 8), the speech area (44) (see Fig. 113), and the parietal visual area (19) are all concerned directly or indirectly with the skilled movements of the hands, mouth, and eyes that develop in the higher mammals. In all, there is a good deal of cortex that nature has given us for organizing mechanisms of manipulative behavior.

ONTOGENETIC DEVELOPMENT OF BEHAVIOR

Comparing the development of the cerebral cortex and that of behavior in evolution gives us one way of looking at the physiological mechanisms of behavior. Another way is to see how behavior develops in the growth of animals of various species. Observations of this kind, together with some physiological experiments, have given us several important facts about the physiological basis of motor patterns.

Maturation of Patterns of Behavior. Several years ago it was still a matter of debate how many of our basic motor patterns are learned and how many are the outcome of physiological maturation. Some of the 'behavioristic' theorists, in their zeal to get away from notions of mind and instinct, went so far as to hold that our simplest reflexes are learned. One theorist, for example, suggested that the grasp reflex is learned (Holt). The way of learning it, he thought, was that spontaneous grasping early in life stimulates the palms of our hands so that the stimulation of the palms becomes associated with grasping. There were similar attempts to explain other reflexes as due to learning. We now know that the largest share of our reflexes and motor patterns are not learned but are a matter of maturation. As the nervous system grows, differentiates, and establishes connections, it provides for just about all the patterns of reaction that we need for the first few months in the world. There are a great variety of experiments that prove this point, but we will mention only a few briefly for illustration.

The classic experiments on this point were done with the pecking behavior of chicks. Pecking responses make a very accurate and at the same time rather complex pattern of motor coordination, which can be readily measured. In a whole series of experiments extending over a period of 30 years, it has become quite clear that the pecking pattern unfolds through physiological maturation (Cruze). Exercise, or practice, has a little to do with perfecting the pattern, but it is not the primary factor. As you might imagine, the experiments were done by keeping some chicks in the dark—so that they could not peck—while control groups were allowed to practice in the normal way. Although chicks kept in the dark are not quite so good when they have their first chance to peck as those with previous practice, they catch up so fast in their performance that it is obvious that the normal improvement in pecking seen in young chicks is primarily a matter of maturation, not learning.

There is a similar experiment on locomotion in the salamander, which will serve as another illustration (Carmichael). One group of salamanders in the very early stages of development—before swimming—was kept in water that had chloretone, an anesthetic, in it. This anesthetic kept them from swimming, but it did not interfere with the normal growth processes. Another group of the same age was allowed to grow up in a normal way. When this group was swimming about very well, the first group was freed of its anesthesia. Within a very few minutes—the time taken for the chloretone to wear off—the first group was swimming just about as well as the other group. Obviously it needed no practice or learning but only time for the patterns of organization in the nervous system to unfold.

Experiments of this sort are much more difficult to do with human beings than with animals, but a number have been done. The story is the same. Even in such patterns as walking and crawling, the rate at which infants acquire them is not nearly so much a matter of learning as it is of the gradual growth and establishment of the proper nervous connections and patterns of function in the nervous system. There are now so many proofs of this point that there is no need to belabor it (see Carmichael).

The Pattern of Development. Most psychologists and physiologists eventually came to see that the basic patterns of coordination and manipulation are not learned but are matters of physiological maturation. Another question then came up for discussion and experiment. It was the way in which behavior patterns mature. Do they unfold by *individuation* or *integration?* That is to say, is behavior first gross and crude, becoming finer and more specific, or do individual reflexes appear first and then become integrated later into patterns of coordinated behavior? There have been many experiments on this question, and the answer seems to depend a great deal on what animal is used in the experiments.

Individuation. The classic studies were made on the salamander (*Amblystoma*) by Coghill. This animal is an amphibian that is rather low in the vertebrate scale. In its development, it is first a "tadpole" without limbs and in that stage begins to swim. Later it grows legs and comes to walk and run. Coghill's very neat experiments with the salamander brought him to the conclusion that behavior patterns develop through *individuation.* The animal first makes gross movements of its whole body, then the more complicated patterns necessary for swimming and walking. So the finer responses follow the gross responses in development.

Integration. After Coghill's experiments there followed many others with different animals. Two of them were with birds. In both cases gross movements appeared very early, but at the same time some rather highly specific reflexes could be obtained in the limbs and other muscles (Kuo; Orr and Windle). Without going into the details let us simply say that such 'mixed' results also were found in such mammals as the rat, the cat, and the guinea pig. In some experiments, in fact, investigators observed some highly specific reflexes as the first items of behavior to make their appearance in development. They therefore held that the course of development was one of *integration,* not individuation (see Carmichael).

It is sometimes hard to see just why different experiments seem to give different results, and in this case they were the occasion for considerable debate. Now, however, after the smoke has cleared away, we can see that the debate and even the issue of integration vs. individuation was largely unnecessary. There appear to be two main factors that determine whether reflexes or gross postural patterns appear first in development. One is the kind of stimulus that is used to test for behavior. Relatively weak stimuli tend to bring out local, reflex behavior; strong stimuli tend to call forth crude movements of the whole body. Carmichael and Smith demonstrated this point well in experiments with bristles that could be applied with different pressures. Secondly, the pattern of development depends a good deal on the species of animal under study. An animal such as the salamander comes into the world with a yolk sac that provides food for a good time. About the time the food runs out, the animal starts to develop locomotion of a swimming type. For a while this pattern is about all that is needed to find food. The salamander, moreover, being a locomotor amphibious animal and low on the manipulative skills, has less use for a lot of specific reactions than do some of the higher animals. In contrast is the guinea pig, which is born at a rather mature level of development—it walks, runs, squeals, and eats at birth. Such an animal, if it is to survive, must develop a rather good repertoire of all sorts of reactions very early.

The salamander and the guinea pig are just two of many possible animals. The upshot of the research, however, is that patterns of behavior mature in different animals, both before and after birth or "hatching," in different ways. There may be a combination of courses of integrative and individuative patterns. Sometimes the first patterns to appear are very crude, sometimes they are highly specific reflexes. The timing of the maturation, however, is characteristic of the species and, in general, of the needs of the animal. Nature sees to it that the physiological growth of the nervous system takes place at the rate and in the order that is necessary for the survival and normal life of the animal.

PHYSIOLOGICAL FACTORS IN DEVELOPMENT

It is interesting to look 'under the skin' of the developing organism to see what changes in nervous structure and function underlie emerging patterns of behavior. Embryologists have now given us a good deal of information on this point (Sperry). By many experiments in which different parts of the nervous system, the sense organs, and muscles are removed or transplanted at various stages in development, they have been able to tell us what factors enter into the development of behavior.

Peripheral Influences on Neural Structure. The salamander makes a very nice subject for studying the embryology of behavior because it is possible to operate on it and make all sorts of removals and transplants of tissue from one animal to another and from one part of the body to another—all with relatively normal growth and function in the excised parts. For this reason salamanders, and particularly the amblystoma, have been used for many years in this type of experiment. Back in 1907, Harrison grafted limbs of salamanders into abnormal positions on their bodies. He observed that the limbs received comparatively normal nerve supply and in some instances came to function "normally" in patterns of behavior. This kind of observation has been confirmed many times in the experiments that followed.

Nerve Supply. Detwiler, for one, carried out a series of researches on the innervation of grafted limbs (see Fig. 124). When, for example, he moved a limb forward or backward from its normal position on the body, he found that the limb in some way attracted nerve fibers to it so that the limb received many of the same fibers from the spinal cord that it would have gotten in its normal position. Similarly, if the normal growth of nerves to a peripheral structure, say a limb, is prevented in some way, as by blocking or removal, nerves from some other part of the spinal cord (usually the nearest possible part) grow out to serve the structure (Hamburger). Sometimes even nerves from the opposite side of the cord grow out to a limb, if it cannot get its normal supply of nerves. Finally, we know that even foreign structures, such as a tail, an eye, or an olfactory bulb, also have some attractive influence, for when they are transplanted to the side of the body, they also get nerves to grow out from the spinal cord to them (Detwiler). All in all, by these and many other experiments, we know that the sense organs and muscles exert some sort of attraction on the nervous system to send out nerve fibers to them (Weiss, Detwiler).

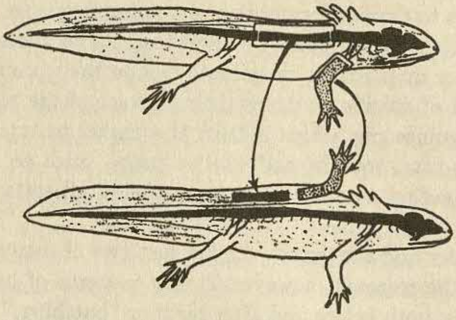

FIG. 124. Showing transplantation of a portion of the spinal cord and of a forelimb from one amblystoma to another. (*From P. Weiss. Autonomous versus reflexogenous activity of the central nervous system, p. 55. Proc. Amer. phil. Soc., 1941, 84, 53–64. By permission of the American Philosophical Society.*)

We know also that the peripheral sense organs and muscles control to some extent the growth of centers within the central nervous system. If, for example, a limb is surgically removed from an amblystoma, the dorsal sensory ganglia serving the limb do not develop to the extent that they normally would. Or, conversely, by grafting on additional limbs, thus increasing the peripheral load, there is a greater growth of the ganglia than usual. In many experiments similar relations have been demonstrated for the brain by removing or transplanting additional sense organs. The appropriate centers of the brain are underdeveloped or overdeveloped, as the case may be. Thus peripheral influences affect the extent to which cells and centers develop within the nervous system (see Weiss, Detwiler).

Intracordal Influences upon Neural Structures. In addition to peripheral factors, there are strong influences of certain centers within the nervous system upon the growth of other tracts and centers. The motoneurons of the spinal cord, for example, are controlled not nearly so much by peripheral influences as by central factors (Carpenter). Moreover, the general growth of the spinal cord seems to be governed to a large extent by the medulla. This has been demonstrated by transplanting the medulla into different positions. The medulla seems to 'decide for itself' how it develops, for its growth in size and pattern tends to go on normally wherever it is put. The medulla, however, tends to control how the spinal cord grows, for when it is transplanted into some position in the spinal cord, the cord just below it tends to develop in the way it would if it were just below the medulla in its normal position. This is just one example; others could be cited. They all indicate that there are intrinsic factors, as well as peripheral ones, that help make the structure of the nervous system.

THE DEVELOPMENT OF MOTOR COORDINATION

How the nervous system forms is only a background question for us. More important is the question of how patterns of behavior are established. There are a good many experiments on the question, and research on it is continuing. We shall give a brief review of the high lights of what we know and do not know about it at present.

Transplantation of Limbs. If the budding limbs of a tadpole are taken at the right stage of development—before the limbs and digits are fully formed—and transplanted to another animal in about the same stage of development, they will graft on readily and grow to become fully formed functional limbs. They attract nerves from the spinal cord and in the course of time begin to move. By comparing the movements of such limbs with those of the other normal limbs of an animal, we can get an idea not only of their individual function but also of how they fit into the pattern of coordination of the animal.

The surprising thing is that the pattern of movement is normal. Whenever the normal limb makes a movement, the grafted limb does, too (Weiss). And if the grafted limb has been attached in the same orientation as the normal one, the pattern of movement will be the same in the two cases. Actually, if we think in terms of the contraction of particular groups of muscles, the flexors and extensors, the patterns of contraction in the grafted limb are the same regardless of the orientation of the limb. Thus if the grafted limb is put on facing backwards, its direction of movement will be the opposite of that in the normal limb—which means that its flexors contract when the normal limb's flexors contract and similarly too with the extensors.

In cases in which grafted limbs have been placed in an abnormal position, either upside down or backwards, the movement of the limb, of course, is not functional. It does the wrong thing to cooperate with the other limbs. Such cases have been observed for long periods of time to see whether there is any change—whether the animal learns to make the "correct" movements with the limb. The answer is that it does not. Animals will go on making the original movements—whether they are functional or are a real detriment to motor coordination—that appeared when the transplanted limbs were first supplied with nerves (Sperry).

The Muscle's Name. There is an important point underlying all these phenomena. It is that muscles get their supply of nerves according to what kind of muscle they are, whether flexors or extensors. As one embryologist (Weiss) has said, "Muscles have their names and the nerves know their names." What these names are, in biochemical or physiological terms, we do not know, but there is some way in which a particular muscle attracts the "correct" nerves from the nervous system, *i.e.*, the kinds of nerves that would normally get to the muscle. Such attraction determines the pattern of motor coordination in the limb regardless of whether the limb is properly oriented or attached and regardless of whether the pattern is "good" or "bad" for the animal.

Knowing this rule about the "muscle's name," we can predict many of the other facts that have turned up in embryological experiments. If, for example, the flexor and extensor muscles are reversed in their attachments in the limb, even before the nerves have grown down to them, the pattern of movement is reversed. The muscles get the same nerves they would have gotten, and since the muscles are now in opposite positions, the pattern of movement is reversed. Similarly, one can interrupt and reorient the nerve supply to a limb, but when the nerves regenerate they tend to establish the "correct" connections with the muscles. These and similar findings can be understood in terms of the muscles having some specific property that controls what nerve fibers, or at least what neural connections, are made with the muscle.

The next question is how and why the muscles get names. Why is it that patterns of motor coordination are determined in embryological growth by the kind of muscles involved in the coordination? There have been many experiments on this question. We do not yet have a specific answer, but we know generally what kinds of factors can or cannot be working in the situation.

Nerve Outgrowth Theory. One possibility is that nerves have "names" and that muscles attract a particular set of nerve fibers regardless of conditions that try to interfere. That is probably not the case. In some experiments nerves have been mixed up rather severely or nerves have grown out to entirely foreign structures, such as an eye placed on the side of the trunk. Nerves seem to grow rather indiscriminately to the sense organs and muscles of the periphery. There certainly is some general attractive influence that makes nerves grow out, but it is highly improbable, in fact impossible in many cases, that particular nerve fibers get to particular muscles (Weiss).

Connectionistic Theory. A more likely possibility is that the muscles "tell" the nerve fibers what connections to establish in the nervous system (see Straus, Sperry). Put another way, each muscle seems to have some biochemical characteristic, the nature of which we do not know. When a nerve grows out to the muscle, the muscle in some way or other gives the nerve some specific characteristic. On the other end of the neuron in the central nervous system, the neuron establishes the connections with the tracts in the nervous system that are appropriate to its function, *i.e.*, the type of muscle with which it is connected.

All this may seem very strange and mystical. Certainly we do not know how the muscles have distinguishing properties or how they communicate the distinction to their nerves so that the nerves make the "correct" connections. But somehow they do. Moreover, although we do not understand it, such specificity is just another case of the sort of phenomenon we meet in sensory functions. There fibers make the "correct" connections with the sensory centers of the brain. They have, moreover, some specific properties that account for our qualities of experience. The problems and the mechanisms, therefore, appear to be the same in both sensory functions and in establishing the patterns of motor coordination.

Higher Animals. There is just one more point to make in this connection. By a host of experiments, not only in amblystoma but in toads, rats, and monkeys, we know that once the basic patterns of coordination are laid down, it is practically impossible to change them (Sperry). If, *e.g.*, we cross nerves to the flexor and extensor muscles in the leg of a rat, we reverse the pattern of movement—just the opposite of what happens early in embryological development. If the muscles are switched in position and the nerves are switched at the same time, the pattern of coordination does not change. There are several other possible experiments that have been carried out (Sperry). The upshot of them all is that the muscles control the connections that neurons make in the nervous system when the nervous system is developing in the embryo. Once these connections have been established, however, they do not change, and it is possible to change patterns of coordination by simply switching muscles or nerves.

THE MECHANISMS OF COORDINATION

Having told what we know about the development of coordination, let us turn our thoughts now to the mechanisms of the brain that underlie coordinated behavior. These have their mysteries, but we are gradually coming to understand them better.

Most of the data on this subject come from the clinical and experimental neurologists. They are primarily interested in the changes in motor patterns that accompany injuries to particular areas and tracts of the brain. As psychologists, however, we are interested not so much in the function of parts of the brain as we are in the neural systems responsible for different aspects of coordination. In the summary that we give here, therefore, we must recast and reinterpret much of the data from experimental neurology. In so doing we run the danger of jumping to conclusions that are not fully warranted or of falsely interpreting different experiments. The reader should realize, therefore, that this summary may not be entirely accurate, but it is the best we can do in making sense of the data as we now have them.

EXECUTION OF MOVEMENT

There are, as we shall see, many factors in coordinated movement and many parts of the brain involved in it. We shall take them up in turn. The first and basic question, however, is how movements are executed. What, in brief, are the neural mechanisms carrying out a coordinated act? The answer to this question, at least in primates and man, centers on the precentral gyrus (area 4), but the answer needs some explanation and qualification.

Phylogenetic Development. We have already noted that motor functions are transferred from subcortical to cortical levels in the evolution of mammals from, say, rat to man. This transfer goes along with the development of manipulative motor ability, and it is important in understanding how movements are executed by the brain.

In rats, cats, and dogs, the motor areas of the cortex are not very highly developed. Neither is manipulative ability. When we remove the so-called motor areas in these animals—indeed, when we remove a very large portion of the cerebral cortex—there is no great lasting effect on motor function. The animals can stand, walk, and get about much as normal animals do. When, however, we remove rather small but circumscribed areas of motor function in the cortex of monkeys, apes, and man, there is a marked paralysis that lasts for a long time. In general, the paralysis is greater in man than in monkeys. Because of the important difference between the primates and lower animals, we should keep in mind that the rest of this discussion refers to the primates.

"Executive" Areas. In the primates, then, we need the cerebral cortex in order for coordinated movements, other than basic postural reflexes, to be carried out. Of all the cortical areas, moreover, we now know that area 4, the so-called motor area or precentral gyrus, is the most important (Bucy, Kennard, Hines). Removal of this area causes relatively severe paralysis. Such paralysis is more severe in man than it is in the monkey. If the lesion is confined to area 4 and does not include the suppressor area 4*s*, the paralysis is a flaccid paralysis, *i.e.*, the muscles involved are relaxed but cannot be moved.

People or monkeys suffering injuries to this area carry their arms or legs limply and are unable to move them no matter how hard they "try." You will remember, moreover, that area 4 is quite stimulable electrically, *i.e.*, various sorts of movements are elicited when electrical stimuli are applied to the motor cortex. From these two facts, therefore—the paralysis resulting from injury and the electrical stimulability—it is fair to conclude that area 4 is the principal executive center for motor coordination.

Unfortunately for the scientist, the brain is not assembled out of many little packages. Area 4 is not the only area involved in the execution of acts, although it is the most important one. We know that there is some overlapping of executive functions with other areas. Some pyramidal fibers, typical of area 4, also come from the postcentral gyrus (somatic area I), and there are most lasting and severe paralyses when the postcentral gyrus is removed along with area 4. There also is probably some contribution from area 6, the premotor area, lying in front of area 4. So the so-called executive area includes not only area 4 but also some regions lying in front of and behind it.

Recovery of Function. If one completely removes areas 4, 4*s*, and 6 as well as the postcentral area and thus takes out all the "executive" areas, the paralysis that results is profound. Indeed, from the motor point of view, a man or monkey in this condition is just about as badly off as a decorticate animal. If, however, a lesion or injury is confined to area 4 or to some portion of the "executive" areas, there is usually rather profound paralysis at first, but in the course of time there is a gradual recovery. In the last section of this chapter we take up the problem of recovery of function, and we shall not consider here why and how it occurs.

There are, however, two interesting points about the recovery following partial lesion of executive areas. One is that recovery is less in man than in the chimpanzee and less in the chimpanzee than in the monkey. This fact is an indication of increasing corticalization of motor functions in the scale of primates. The other point makes a distinction between locomotor and manipulative behavior. At first after a lesion the animal may not be able to use its leg or arm in moving about. After a time, however, locomotor abilities return. The person or animal is able to walk again or to use the arm for support. Much slower to return, however, are the manipulative abilities—ability to pick up objects with the hands, to use a pencil in writing, to operate a typewriter, and so on. In fact, if the lesion is severe enough, these manipulative abilities may never return even though locomotor abilities do. Thus we see the progressive development and transfer of manipulative abilities to the cerebral cortex distinguished in the functions of the motor "executive" areas.

Subareal Organization. We have already seen that the motor areas of the cortex are arranged topographically. There is an "arm area," a "leg area," a "trunk area," and a "face area." These areas have been established in a number of ways—by studies of degeneration of fibers, by electrical stimulation, and by firing the cortex with strychnine. It is interesting to see how these areas participate in motor coordination (see Bucy).

As one would expect, removal of the arm area of the motor cortex causes some paralysis of the arm. Similarly, some paralysis of the leg follows removal of the leg area. It is interesting, however, that these areas are not entirely independent. It has been well established, for example, that removal of the leg area in addition to the arm area causes a greater paralysis of the arm than does removal of the arm area alone. And in general we can say that removal of a large portion of the motor area causes greater paralysis of any particular part of the body than removal of only the subarea representing that part. So there is a real collaboration and overlapping of executive functions, even though they are to a large degree segregated into areas (*cf.* homunculus, page 281).

Bilateral Organization. A similar principle holds for the two sides of the brain (see Bucy; Ades and Raab). The motor areas and the pyramidal system are almost entirely crossed; *e.g.*, taking out the arm area from the left cortex causes paralysis of the right arm. There is, however, some bilateral overlap, so that removal of the arm area on both sides causes a more profound paralysis of the right arm than removal of only the left arm area of the cortex. Similarly, there is more rapid recovery from a lesion on one side if the corresponding area on the other side of the cortex is intact than if it has been removed. So although the executive functions are largely segregated according to the side of the body represented, they are not entirely so.

THE COMPOSITION OF MOVEMENT

Although the motor area and the pyramidal system are the route by which movements are initiated by the cortex, they are by no means the only parts of the brain involved in motor coordination. It is possible, in fact, to distinguish different aspects of motor coordination and to point out various centers and pathways responsible for them. One important aspect of motor coordination is the composition of movement, *i.e.*, the sequence and pattern of movements making up an act. There are two areas of primary importance in the composition of movements: the premotor area and the neocerebellum.

Premotor Area. As we have already seen, the premotor area (area 6) lying in front of the precentral gyrus is part of the extrapyramidal system, in fact, the most important part of the extrapyramidal cortex. This system, as we have seen, is concerned in the postural reflexes, but since posture and movement are inseparable, it is also concerned in the integration of movements into coordinated acts.

That the premotor area contributes a good deal to the composition of skilled movements can easily be seen by removing it. Without the premotor areas, either the monkey or chimpanzee shows a good many deficits in skilled movements. For one thing, the animal requires a good deal of practice to reacquire proficiency in manipulatory movements that it acquired preoperatively, say, in solving a problem box (Jacobsen). Some abilities are never completely regained. In such a pattern of behavior as, *e.g.*, grooming, there is marked impairment. The animal is very awkward in attempting to remove fleas from the body, and it particularly has difficulty in coordinating the thumb and index finger as this should be done in grooming. In man, too, injury to the premotor areas causes awkwardness of movement and a very prominent difficulty in approximating thumb and index finger and in making the adjustments in buttoning a shirt or fingering a musical instrument (Kennard *et al.*).

Neocerebellum. The entire cerebellum is concerned in one way or another with the motor aspects of behavior (see Bailey, Fulton). Some of it, however, especially the paleocerebellum—the oldest part phylogenetically—is concerned with postural reactions that we have considered before. The most important part of the cerebellum for motor coordination is the dorsal lobe or neocerebellum. This is the newest part from an evolutionary point of view, and it is highly developed in the primates.

The neocerebellum contributes in several ways to motor coordination, but one of the ways is like that of the premotor cortex. It contributes to the composition of movement. As you might expect, its functions show up most clearly when it is removed either experimentally in monkeys or chimpanzees or by injury in man.

Disturbances in the pattern or composition of movement are particularly apparent in neocerebellar lesions. If a patient with such a lesion is asked to bring his finger from a position above his head to the tip of his nose, he may move his shoulder and upper arm before he begins to flex his elbow—which is an awkward thing to do. If asked to put one heel on the opposite knee, he may bend his hip completely before he bends his knee. Thus he raises his heel much too high and lowers it to his knee. On attempting to feed himself, a patient may first fix his elbow firmly to the side and move the spoon to his mouth bending his elbow only. Frequently such a patient holds his arm or leg too rigidly in attempting to reach out and touch an object.

These are just a few examples that have been reported in the clinical and experimental literature. With lesions either of the premotor cortex or of the neocerebellum it is hard to say just what it is that is wrong. In either case, however, the various component movements that make up a coordinated act are not put together in the correct way. Both these areas, we know, have their fibers connecting with the motor areas of the cortex. These connections apparently are responsible for helping in the organization of movements into coordinated patterns.

THE FACILITATION OF MOVEMENT

We have seen so far that movements are executed by the motor area and pyramidal system but that their composition is controlled in part by the premotor area and by the neocerebellum. It is also important to note that there is some general facilitation of movement offered by these parts of the brain.

The Premotor Area. If the premotor area is removed from a monkey or chimpanzee, the animal shows a pronounced weakness in the limbs of the side opposite the lesion. This weakness is called ***hypotonia.*** The animal appears to be reluctant to use these limbs, and when it does it holds them and uses them in peculiar postures. In time there is recovery and the hypotonia and weakness go away. It is clear, nevertheless, that the premotor areas contribute some "tone" or general facilitation of coordinated movements.

The Neocerebellum. Contributing in a somewhat similar fashion is the dorsal, or neocerebellar, lobe of the cerebellum (see Fulton). This part of the cerebellum sends a cerebellocortical pathway to the precentral cortex. That this pathway continually influences events going on in the motor area and pyramidal pathway is shown by the fact that electrical excitability of the motor cortex is markedly altered when the neocerebellum is stimulated. This connection can also be demonstrated in behavior. When the neocerebellum is removed, one of the signs, among others, is a hypotonia, or weakness of movement. In the chimpanzee, for example, when the animal is walking after neocerebellar lesion, its leg on the affected side lags behind the leg on the normal side. Or when it feeds, it moves its limbs more slowly and more deliberately than a normal animal.

So both the premotor area and the neocerebellum contribute tone, or facilitation, to the motor area in coordinated movements.

THE RESTRAINT OF MOVEMENT

Probably the most important of all factors in coordinated movement is restraint or inhibition. There are several different factors at work in motor coordination that fit in this category.

Kinesthesis. We have already seen how kinesthetic afferents are involved in reflex behavior (see page 308). Through their inhibitory influences, they keep reflexes from starting or stopping too abruptly and generally smooth out the reflex to make it better serve its purpose. Kinesthesis plays a similar role in voluntary behavior.

In man or primates, injury to the kinesthetic pathways, thus cutting off kinesthetic influences to the brain, causes severe disturbances of motor coordination called *voluntary ataxia.* Individuals suffering from such a disorder have trouble, for example, in feeding or in making other rather specific coordinations. Their limbs usually shoot rather wide of the mark and in general look as though "they do not know where they are going." That is because the kinesthetic impulses are necessary to guide a coordinated movement.

The disturbances that we see when kinesthesis is lacking affect different limbs and parts of the body in different amounts. The effects are what we might predict from the homunculus (see page 281), which represents the amount of motor cortex assigned to various movements. In general, the parts of the body, like the mouth, face, and fingers, that are most involved in precise coordination are affected most by loss of kinesthetic impulses. Impairment is slight in the hip, more marked in the distal joints, and so great in the digits that these are virtually useless. It is easy to show, however, that there is nothing wrong in the executive pathways of the pyramidal system, for electrical stimulation of these pathways will elicit the movements that normally can be obtained (Mott and Sherrington). What the motor cortex lacks, apparently, is adequate information concerning the events taking place in the muscles.

The neurology underlying the role of kinesthesis in motor coordination is not so simple as we might expect (see Dow). We know that fibers of the kinesthetic system project directly to the motor cortex (area 4), and we also know that the postcentral gyrus, which is the main cortical area receiving kinesthetic impulses, is also involved in the executive functions of the motor cortex. Thus there is direct kinesthetic information being supplied to the pyramidal system at all times. In addition, however, some of the kinesthetic influences in motor coordination undoubtedly are carried by way of the cerebellum. This organ was once called the "great proprioceptive ganglion." Although such a description overstates the case, kinesthetic impulses do make their way in large numbers to the cerebellum, and the cerebellum in turn exerts its influence on the motor cortex.

The Pyramis. Just in passing, we may note the restraint imposed by the pyramis. This is part of the posterior lobe of the cerebellum. When it is removed in the monkey, a rather specific and surprising deficit in behavior appears (see Fulton). The monkey seems unable to coordinate its visual perceptions with its locomotor behavior. It will crash headlong into a wall or clearly visible object. Thus the pyramis seems to contribute to the visual guidance of locomotor behavior. This fact is not well understood. It is interesting that electrical stimulation of the pyramis gives movements of the eyes. Apparently it is somehow concerned in the coordinating of visual and kinesthetic impulses so that behavior can be restrained in the right amount at the right time.

Neocerebellum. For the third time we have occasion to mention the neocerebellum in connection with motor coordination. In the other two cases, we noted that the neocerebellum facilitates the activity of the precentral cortex and also that it contributes to the composition of movements. This time the point is that the neocerebellum is also concerned in the restraint of movements. In fact, unrestrained movements that are excessive in range are about the most easily recognized sign that there is a disorder of the neocerebellum. For example, when a patient with a neocerebellar lesion attempts to touch his finger to his nose he is likely to strike his cheek violently (Holmes). Or a monkey when walking may lift its foot entirely too high from the ground or put it down too violently. These are just two examples. The general point is that the neocerebellum when functioning normally contributes impulses that restrain excessive movements and make them more precisely timed and coordinated.

Tremor. When people try to thread needles or make any extremely fine movement, their fingers or hands usually tremble a little. When they get excited or emotionally upset they may tremble a lot. Ordinarily, however, they do not tremble much—if they are normal—but in certain kinds of injuries to the nervous system there is a great deal of tremor in coordinated movements. By studying the conditions under which extreme tremor takes place, neurologists have been able to tell us something about the mechanisms of motor coordination, particularly those having to do with restraint (see Bucy).

Kinds of Tremor. Two different kinds of tremor appear in diseases of the nervous system. One is *tremor at rest.* Neurologists frequently see it in Parkinson's disease, which involves many subcortical lesions in the brain. The tremor at rest develops when the patient holds his hands or head still, but it disappears whenever a voluntary skilled movement is made. The other kind of tremor is *intention tremor*. It is a very conspicuous tremor that appears only when a skilled movement is made, and it disappears when the hands or head are at rest. This tremor, as we shall see, is the result of injury to the cerebellum.

Mechanisms of Tremor. Tremor, whenever it occurs, is the fault of the motor cortex and the pyramidal system. Impulses traveling down this system, if not subjected to any restraint or smoothing, are synchronized in waves. These waves correspond to the frequency of the tremor. There are, however, probably three different ways in which the 'tremorous' impulses of the pyramidal system are smoothed out.

One is through the extrapyramidal system. The impulses leaving both the premotor cortex and the parietal lobes in the extrapyramidal system appear to be unsynchronized. When these impulses reach the motoneurons of the spinal cord where the pyramidal pathways end, they smooth out the intermittent effects of the pyramidal pathways.

A second smoothing or restraining influence seems to be a circuit in the brain that starts at the precentral cortex, passes down to the substantia nigra, then back up to the basal ganglia, then to a nucleus of the thalamus, and thence to the precentral cortex (see Fig. 125). As we shall see in a moment, there are several circuits of this kind that make up inhibiting and restraining mechanisms in the brain.

There is another circuit between the precentral cortex and the cerebellum (Fig. 126). It passes from the motor area to the pons, thence to the cerebellar cortex, out of the cerebellum by a relay in the dentate nucleus, through the red nucleus, and then by a relay in the thalamus back to the precentral cortex.

Neurologists and physiologists have pieced together these mechanisms from various kinds of data—from cases of lesions in human patients, from anatomical methods of tracing pathways in the brain, and from various electrical and drug methods. They are not sure of every detail nor of exactly how the mechanisms work. Some tentative conclusions seem justified, however.

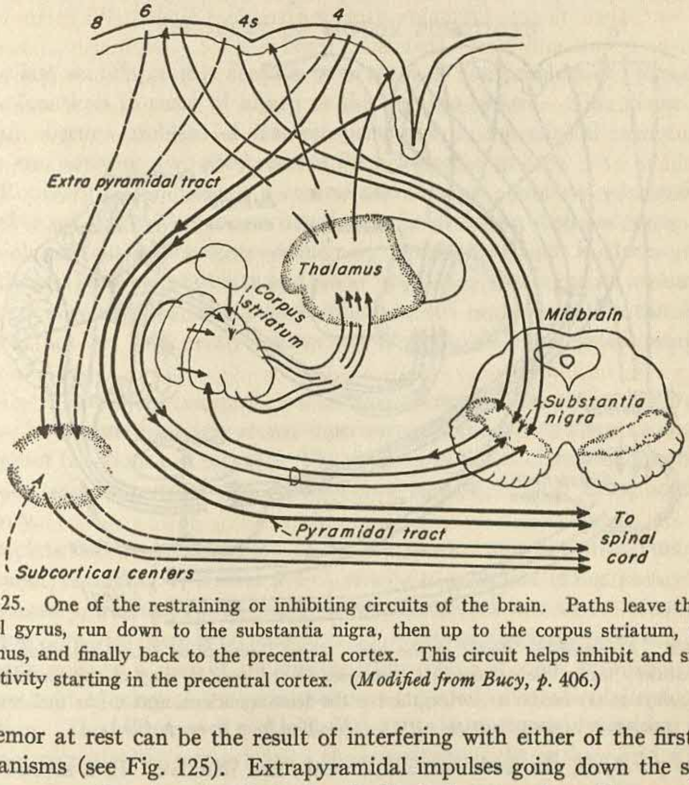

FIG. 125. One of the restraining or inhibiting circuits of the brain. Paths leave the precentral gyrus, run down to the substantia nigra, then up to the corpus striatum, to the thalamus, and finally back to the precentral cortex. This circuit helps inhibit and smooth out activity starting in the precentral cortex. (*Modified from Bucy, p.* 406.)

Tremor at rest can be the result of interfering with either of the first two mechanisms (see Fig. 125). Extrapyramidal impulses going down the spinal cord can smooth out and restrain the rhythmic impulses from the precentral cortex. Moreover, it appears that the circuit from the precentral cortex through the substantia nigra and back again can also restrain the rhythmic tremor produced by pyramidal impulses. Lesions in the brain that interrupt one of these pathways can produce tremor at rest, and that is why we see it in Parkinson's disease.

Intention tremor, we can be rather sure, is due to injury to the third mechanism—the one making a circuit between the motor cortex and the cerebellum (see Fig. 126). The clinical neurologist, when he sees a patient with intention tremor, knows that there is something wrong in this circuit. As one might guess from the circuit, injury to the dentate nucleus of the cerebellum, through which the impulses flow from the cerebellum to the cerebral cortex, produces an intention tremor.

Spasticity. Still another mechanism of restraint can be seen in certain kinds of paralysis. We have already covered well the types of lesions in and around the precentral cortex that produce a motor paralysis. What we did not bring out, however, are the different kinds of paralysis that may occur. In one type, *flaccid paralysis*, the limbs are limp, weak, and inactive. In a second type, *spastic paralysis*, the muscles are rigid and tense. Particularly are the extensor muscles spastic and contracted.

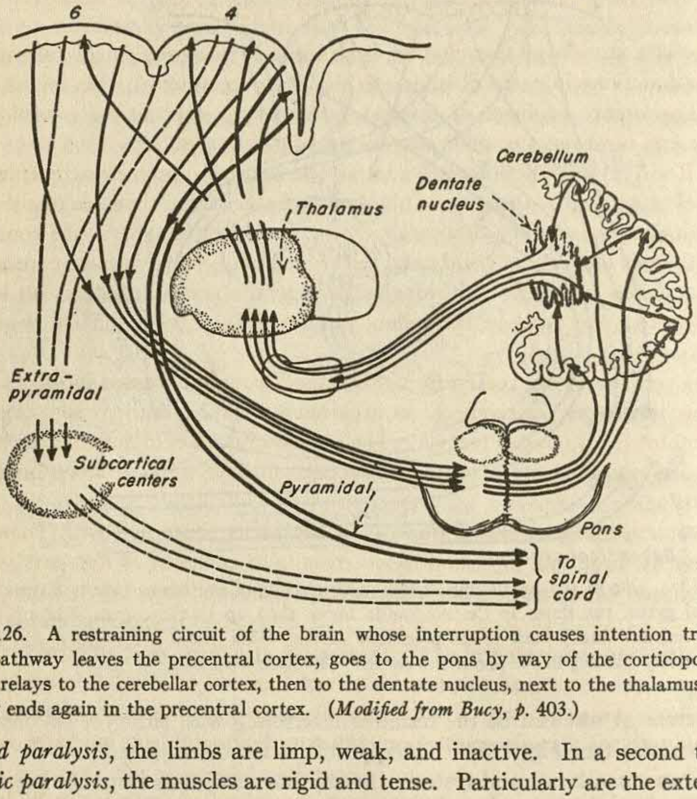

FIG. 126. A restraining circuit of the brain whose interruption causes intention tremor. The pathway leaves the precentral cortex, goes to the pons by way of the corticopontine tract, relays to the cerebellar cortex, then to the dentate nucleus, next to the thalamus, and finally ends again in the precentral cortex. (*Modified from Bucy, p.* 403.)

Neurologists still are not positive of all the reasons for the different types of paralysis (see Bucy). In general, it looks as though lesions of only area 4 or of the pyramidal system cause flaccid paralysis. Spastic paralysis occurs most often when area 6 or parts of the extrapyramidal system are damaged. It is particularly prominent when the suppressor area (4*s*) is damaged in addition to areas 4 and 6. It is thus clear that the extrapyramidal system, and particularly the suppressor area (4*s*), exercises restraint on impulses arising in lower centers (Hines). Undoubtedly the mechanism is related to that of decerebrate rigidity with which we dealt somewhat earlier.

By now we have seen a number of restraining mechanisms that are necessary in motor coordination. There are still others that we have not mentioned (see Obstinate Progression, page 376), but there is no need to go into them. The important point is that many of the coordinated aspects of behavior are the result of various restraining mechanisms.

RECOVERY OF MOTOR FUNCTIONS

The last section of this chapter is devoted to the problem of recovery of motor functions in cases of injury to the nervous system. This might seem like an obscure problem of interest primarily to the clinical neurologists. There are, however, two good reasons for bringing it up here.

1. Recovery of functions is a central and annoying problem wherever and whenever we deal with nervous functions. Later on we shall see many cases in which nervous injury destroys memory and learning, yet in the course of time there is recovery of ability and relearning. It is only when we understand why and how abilities lost through injury to the nervous system can be recovered that we shall really understand how the nervous system works in behavior.

2. There is another reason for considering recovery of motor functions, *viz.*, that we have some relatively recent experiments that begin to give us some idea why motor functions can recover. The progress in this field may help us better to understand recovery of memory functions (see page 505). Here, briefly, is the story.

Complete bilateral extirpation of all the areas concerned with voluntary movement, including 4, 6, and 3–1–2, results in complete motor paralysis of all voluntary movements in man, chimpanzee, and monkey. From such profound paralysis there is no recovery. If, however, the experimental injuries are made only to a part of the crucial areas, there is some improvement in function and effacing of the paralysis over a period of months following the operation. This recovery of motor functions has been known for a long time, but only recently has research been throwing some light on how and why it occurs.

Postcentral Gyrus. One study shows that the postcentral gyrus (3–1–2) may be responsible for some recovery after the removal of the precentral (area 4) cortices (Ades and Raab). Ordinarily, when the motor cortex is removed simultaneously on both sides, a rather profound paralysis results. If, however, a lesion is made only on one side and a period of three or four months is allowed before taking out the other side, we do not get the usual paralytic signs of bilateral injury. Obviously there has been compensation taking place between the removal of one cortex and the second operation. Moreover, this compensation must involve some areas other than those of the motor cortex (area 4). It turns out that the postcentral gyrus (3–1–2) is responsible for this compensation, for if it is also removed along with the extirpation of the corresponding precentral cortex, paralysis occurs after the second operation just as it would have if both sides had been removed simultaneously in one operation.

Injury in Infancy. We see the work of compensation in comparing the effects of cortical removal in infant monkeys (Kennard). It is interesting that when cortical areas 4 and 6, the motor and premotor areas, are removed from infant monkeys, there is very little immediate effect on motor performance, *i.e.*, there is no paralysis. As time goes on and the monkeys grow older, some signs of paralysis make their appearance, but these are much more moderate than if the injury were made in adult monkeys. From this study it is possible to draw several conclusions. Some kind of reorganization of brain functions goes on after the removal of the motor areas; this reorganization is greater in the young monkey than in the mature animal, occurring to the greatest extent in the first six months of life. Apparently the parts of the cortical motor system that remain are responsible for the reorganization.

To test this hypothesis, Kennard and her colleagues have carried out an excellent set of experiments. They make use of three distinctly different methods for determining what reorganization has taken place. One method is the use of a stimulant during the period of recovery following the operation. A second is the use of a sedative, and a third uses a test of the electrostimulability of the cortical areas before and after the operation.

Stimulants. The stimulant used was strychnine (Ward and Kennard). This is a well-known nervous stimulant and probably acts by interfering with cholinesterase activity at the site of transmission of nervous impulses. Ward and Kennard also used two other chemicals that are known to have a stimulating action on the nervous system: thiamin (vitamin B_1) and doryl. By using these drugs postoperatively, singly or in combination, they observed that all animals suffering removal of the cerebral cortex on one side were aided considerably in both the rate and degree of recovery of their motor functions. She concluded that this increased rate of recovery was due to the fact that the stimulus accelerated the rate of functional reorganization in the parts of the motor system remaining after operation.

Sedatives. The opposite result was observed with the use of sedatives (Watson and Kennard). Several monkeys were deprived of their motor and premotor cortices (areas 4 and 6) on one side and were treated with sedatives such as phenobarbital and dilantin during the postoperative period. It turned out that phenobarbital, in doses so small that they had no observable effect on the cage behavior of the monkeys, produced a very marked slowing in the rate of recovery of motor functions. In fact, the animals never reached a level of recovery typical of other monkeys subjected to this lesion without the use of sedatives. The experimenters concluded that the sedatives interfered with the reorganization of remaining tissues of the cortical motor system.

CHAPTER XVI

EMOTION

Feeling, pleasantness, unpleasantness, and, in general, the sensory aspects of emotion were covered in an earlier chapter on somesthetic experience. Here we shall emphasize the behavioral aspects of emotion. First we shall consider some of the problems and difficulties in studying emotion. Then will follow sections on autonomic aspects of emotion, the lower centers and emotion, the hypothalamus and emotion, and the cerebral cortex and emotion.

THE PROBLEM OF EMOTION

Emotion is a difficult topic. It covers not only how organisms act but also how they feel. It includes a great variety of patterns of behavior and of feeling. As a consequence it has been hard to arrive at a good classification of emotions, really conclusive and quantitative experiments have been few and far between, and there has been a great deal of argument and confusion about theories of emotion. It seems fitting, therefore, that we devote some time to the problem of emotion before presenting some of the specific experimental facts that we now have available.

Emotional Behavior. There are a great many kinds of behavior included under the term *emotion*. Some involve primarily the somatic musculature. In man, for example, some of the somatic emotional reactions are smiling, laughing, crying, screaming, running (in fright), startle responses to sudden loud sounds, and various facial expressions of emotion. In animals we see some of these same reactions, but we also see such patterns as snarling, purring, yelping, tail wagging, the baring of fangs, hissing, and certain patterns of facial and bodily reaction that go along with them. Obviously the topic of emotional behavior takes in a great gamut of somatic reactions.

In both man and animals there are a variety of autonomic reactions that are a part of emotion. There is the pallor of fear in which blood tends to leave the head. There is fainting, which is a more extreme case of circulatory change accompanied by loss of consciousness and changes in bodily posture. Increases or decreases in the heart rate or in blood pressure occur in emotion. Secretions of various glands may be increased or lowered with resulting changes in the metabolism of the body. These, briefly, are a few of the autonomic emotional reactions.

Emotional Experience. People and animals not only act emotional; they "feel" emotional. People give us verbal reports of such emotional experiences, while we can only infer them from the behavior of animals. There are, moreover, all shades of emotional experience. We may feel 'afraid,' 'mad,' 'happy,' 'excited,' 'depressed,' 'quiet'—such words could be multiplied almost indefinitely. Because of all the patterns and shades of emotional experience, it has been very difficult to work with it scientifically or, more specifically, to get at its physiological basis.

In a previous chapter (Chap. XII), however, we outlined some of the mechanisms of internal sensation. We saw that there are receptors of all sorts associated with our autonomic effectors and their related tissues. Pain receptors are liberally distributed in blood vessels. Pressure receptors are included in many of the smooth muscles and internal tissues. We have, of course, the various kinesthetic receptors in the somatic muscles to record tension and relaxation. So even though we cannot outline specific mechanisms for various shades of emotional experience, we can be rather sure of their basis. There is a continual inpouring of sensory impulses from within our body, and these are what we "feel."

Theories of Emotion. Emotion has been the subject of a lot of theorizing, and the theories that have been concocted have concerned all aspects of emotion (Ruckmick, Young). Some theories have been concerned with the evolutionary development of emotion and how it serves the interest of survival. Some have speculated about the parts of the brain that might be involved. Others have dealt with the stimuli and the causes of emotion.

The theory that held the stage for many years and is still famous was put forth by Lange and James (see page 254). What the theory attempted to explain, in general terms, was how emotional behavior and emotional experience are interrelated physiologically. At the time of its popularity, little was known about specific brain mechanisms. The important point that it made was that emotional response comes first and emotional experience is the result of response. As James saw it, an emotional stimulus sets off autonomic responses in our blood vessels, glands, and so on, as well as in skeletal effectors. These responses act as stimuli for internal receptors, which send impulses back into the nervous system. These impulses give rise to emotional experience. Thus, said James, "We are afraid because we run; we do not run because we are afraid."

The James-Lange theory has been much maligned in recent years. Many elementary textbooks, in fact, talk as though the theory had been disproved and another theory, the Cannon-Bard theory, had been put in its place. That is not quite the case. What did happen is this. Cannon and his coworkers prepared cats in which the sympathetic system was sectioned along the whole length of the spinal cord. Such animals do not give the autonomic responses that are part of the normal animal's emotional behavior. Yet these animals are able to give the hisses, snarls, spits, and facial expressions of an angry or fearful cat.

The fact that sympathectomized cats show all the outward signs of anger, yet cannot "feel" it—at least in their autonomic system—has been held up as evidence against the James-Lange theory of emotion (Cannon, Bard). So also have some data met with in clinical patients (Bard). For example, there are sometimes cases of people who have pathological laughing or crying and who may not feel at all the way they act (Wilson). They may feel sad when they are laughing uproariously or weep when they feel hilarious. There are frequently cases in which the expression of emotion is impossible because of facial paralysis, yet these people feel emotion. So it is clear that there is no one-to-one relation between our responses and what we experience. In this respect, then, the James-Lange theory is not entirely correct.

The matter of a good theory relating emotional behavior and emotional experience, however, is not settled (see Hunt). There is no proof that autonomic responses do not determine how we feel. There is only evidence that we may be able to feel in the absence of internal responses or feel something that does not go along with our facial expression. It is a matter of common sense, however, that pressures, pains, and other sensations in our bodies have something to do with the way we feel. Moreover, emotional responses can "work us up into a state" so that we come to feel bad. Yet feelings seem to be possible without responses. So there the matter must rest for a while.

Types of Emotional Response. One of the problems that haunts students of emotion is how many kinds and classes of emotional response there are. It is certainly clear that emotional patterns develop slowly in infants during the first year (Bridges). At first it is very hard to tell one emotional pattern from another. Even in adults many studies indicate that we have great difficulty telling from an emotional response just what type of response it is. We generally need to know the situation as well as the emotional response in order to name the emotion.

Although there are many variations in emotional patterns, in animals below man the patterns seem to be grouped into three basic categories: rage or anger, fear or withdrawal, and pleasure or friendliness. There are other names for the triad of emotional patterns, but most observers feel that the three patterns are easily identified, at least in such animals as the dog and cat. Moreover, the patterns in these animals do not seem to depend in any way upon training or culture. Instead, the patterns appear to be inborn reactions that appear fully expressed when the proper stimulus for them presents itself.

So it is hard to know just how many emotional patterns there are, how much they are inborn, and how much they are culturally modified in man. Perhaps this is a case in which instinctive patterns that are highly developed in lower animals die out as we ascend the mammalian scale, leaving patterns more and more to the influences of learning and culture. We shall see in a later chapter that this is partly true of sexual patterns. For our present purposes, it is well to assume that there are three basic patterns of response corresponding to fear, anger, and pleasure. Even if these are not true physiological entities, they serve as a set of coordinates in which to take up the physiological problems of emotion.

AUTONOMIC ASPECTS OF EMOTIONAL BEHAVIOR

It takes only a brief look at what happens in the body along with emotional reactions to see how important the autonomic system is in such behavior. This system, which is a means by which the organism looks after its internal environment, is almost always thrown into some kind of an uproar when an emotional stimulus comes along. Especially in rage and fear do we see autonomic reactions. The reactions, in fact, are the kind that are necessary to prepare the organism for action and for energy expenditure. For that reason Cannon and Bard, the most prominent research workers in the field in recent years, have been stressing the *emergency functions* of emotion.

Peripheral Effects. Much of the work on autonomic aspects of emotion has been done with rage and fear, because they are so easily induced in animals (Bard, Landis). Most of the autonomic effects under these circumstances are sympathetic, as we can see by taking a brief look at them. There are changes in the alimentary tract—which are too complex to go into—but they represent the typical pattern of sympathetic discharge to the tract. Salivation is restrained or stopped—as anyone who has had stage fright will probably remember. Movement of the stomach, secretion of gastric juices, and peristaltic movements of the intestine are all inhibited. These effects, incidentally, slow down or halt digestion. The colon and bladder do not empty as easily as normally, and constipation may be the result. In some situations, however. when sympathetic effects have a rapid onset, there is a brief compensatory outflow of parasympathetic impulses, giving rise to defecation and urination. This will happen, for example, in the rat when placed in strange surroundings, and it is sometimes taken as a measure of emotionality (Hall).

Like the activities of the alimentary tract, there are changes of the circulation in rage and fear that are predictable by knowing the effects of sympathetic discharge (see Hunt). Sympathetic impulses to the heart, you may remember, make the heart beat faster. Because sympathetic impulses constrict the larger blood vessels and the vessels of the gut, blood is taken away from the skin and viscera and sent in the direction of the muscles and the brain—which presumably will need it in an emergency. Speeding up the heart rate and constricting blood vessels at the same time makes the blood pressure go up. The net result of these changes in fear and rage is that the body stops its processes of storing and digesting food and mobilizes its resources for the expenditure of energy.

Cerebral Blood Supply. In the emotional reactions of people, we often can see changes in the distribution of blood to the head (Lund). At one extreme is the blushing of shame or embarrassment and the flush of rage; at the other extreme is the pallor of fear. These changes come about because of dilation or constriction of the blood vessels leading to the face and head. In some instances the effects are so pronounced that they lead to fainting. This, in general, is due to such general dilation of blood vessels in the body that all the blood leaves the head, depriving it of oxygen and causing loss of consciousness.

This kind of reaction—the one in fainting—can come about directly or by way of a compensatory reaction to sympathetic discharge. Suppose, for example, that the blood pressure rises very rapidly because the sympathetic system is thrown into play. The rapid rise in pressure can stimulate receptors for pressure in the carotid sinus and thereby bring reflexes into play in which the parasympathetic system discharges. As a result there is a general expansion of blood vessels, slowing of the heart—sometimes to a standstill—and greatly reduced blood pressure.

Chemical Effects. The sympathetic reactions that we see in emotion express themselves not only in reactions of the smooth-muscle effectors but also in changing the chemical and endocrine balance of the blood (see Fulton *et al.*). One of the most prominent cases of this action is the release of adrenalin from the medulla of the adrenal glands. Adrenalin, as we have already pointed out (page 96), mimics the action of the sympathetic system. When it is circulated in the blood, it produces the same general effects as do sympathetic impulses. It causes the heart beat to speed up, and it causes the glycogen in the liver to be converted into sugar and released into the blood stream, thereby raising the blood-sugar level to meet the requirements of great energy expenditure by the brain and muscles. Adrenalin also stimulates the thyroid gland to greater efforts and in this way increases general oxidation in the body. Thus, through the secretion of adrenalin and its effects, important changes in the internal environment of an individual take place when he gets emotional.

There is one set of experiments that points up the relationships between endocrine glands and emotional behavior in a striking way (Hall; Yeakel and Rhoades). The experiments show that there is a close connection between the glandular make-up of the organism, its genetic constitution, and emotional expression. First, certain standard tests were developed through which emotional and fearless rats could be distinguished from each other. These tests employed defecation and urination in controlled situations as measures of emotionality, and they measured the readiness with which animals give their emotional responses in strange situations. The two kinds of animals—the fearful and the fearless—were kept apart, and by controlled breeding, strains of fearless and of emotional rats were obtained. Then the glands of the animals were studied. The emotional rats, it turned out, had considerably larger adrenal, thyroid, and pituitary glands than did the fearless rats. Thus is emotionality correlated with constitution and, indeed, by inference, with an internal environment that must be considerably different from that of the less emotional animal.

General Sympathetic Effects. There are still other sympathetic effects that appear in emotion (see Bard). We can mention them briefly. For one, the sweat glands of the skin, which are under sympathetic control, secrete their fluid and thereby prepare the way for the disposal of large amounts of heat that may be set free in emotional activity. The muscles at the bases of the hair follicles contract. Thus the hairs are erected and "goose pimples" form. Profound changes in respiration may also take place, but these follow no set pattern. Gasps, catching of the breath, panting, and labored breathing are some of the variants of emotional breathing. One change connected with respiration that regularly occurs under sympathetic influences is dilation of the bronchioles of the lungs. In this way the rate of exchange of oxygen and carbon dioxide in the lungs is stepped up to a considerable degree. One final physiological effect to mention is the release of red corpuscles from the spleen, where they are ordinarily stored. With an increase of these corpuscles in the blood, the oxygen-carrying capacity is raised accordingly.

THE LOWER CENTERS AND EMOTION

In many aspects of behavior, we find that the data we get from human beings is rather unsatisfactory. Emotional behavior is no exception. We have the usual limitation, of course, that the natural lesions or injuries to the brain that occur in people often are not placed where we would like them to be for us to draw conclusions. Moreover, as usual, we often cannot be sure exactly where they are. Finally, emotional patterns are so complicated and so diverse that our clinical descriptions are difficult to interpret.

Emotions in Animals. Animals, particularly the dog and cat, are much more suitable for research on the physiological basis of emotion (see Bard). For one thing, their patterns of emotion are much easier to identify. The *rage* reaction of the dog, for example, consists of lashing of the tail, arching of the trunk, thrusting and jerking of the limbs, protrusion of the claws and clawing movements, snarling, movements of the head from side to side, attempts to bite, and very rapid, panting respiration. A somewhat similar and definite description can be given for rage in the cat. The *fear* reaction in the cat is displayed by dashing off in a furtive or precipitate manner, mewing plaintively, trembling, and taking cover behind any available object. The *pleasure* reaction in dogs and cats is familiar to the layman. Its most evident sign in dogs is tail-wagging and in cats it is purring. Other reactions such as those to petting and stroking are also signs of pleasure. These various patterns of emotional reaction make it practicable to study emotion in such animals as dogs and cats.

In animal studies it is possible to get a crude idea of the *threshold* of emotional response. How hard the tail must be pinched to elicit a rage reaction, how much of a threatening gesture must be made to provoke fear or rage, how readily an animal comes to the experimenter for stroking and petting, and other similar signs have been taken to indicate changes in the *threshold* of emotional response. Such thresholds are very crude, but when we come to make comparisons of the functions of different parts of the nervous system in emotion, the notion of threshold is useful.

Finally, of course, we may note the usual advantage of using animals. We can make lesions of the nervous system where we want to study the function of particular parts, and we can then make careful post-mortem checks of the damage done. In this way it is possible to correlate changes in behavior with definite effects on the nervous system.

The Spinal Cord and Medulla. Now we are going to consider the function of different parts of the nervous system in emotion. We shall begin with the lower parts and work up gradually through the higher centers of the brain. In general, of course, the method has been to section the brain stem at different levels or to remove particular parts to see what the effects on behavior are.

One thing that is quite clear is that the autonomic aspects of emotional behavior can take place at the spinal level. Sympathetic responses occur in a spinal animal to all sorts of noxious stimuli, such as pinching, cutting, or shocking. The bulbar animal, *i.e.*, one with the medulla and spinal cord intact, gives a somewhat more coherent picture of autonomic response than the spinal animals, for the centers for respiration and circulation are found in the medulla. In bulbar animals, therefore, we find various sympathetic and autonomic reactions to certain kinds of emotional stimuli, such as pinching, jostling, and, in general, somesthetic stimuli.

In addition, of course, to autonomic responses, there are the somatic emotional patterns to consider, too. Moreover, there are questions about the kind of stimuli and the intensity of stimuli required to produce emotional reactions. In discussing the other aspects of emotional response, it is well to consider the medulla, pons, and midbrain together, for they have been studied together in experiments and it happens that there are comparative conclusions to be drawn concerning them.

Medulla, Pons, and Midbrain. At one time there was some dispute about emotional patterns to be seen in dogs or cats with nothing above the midbrain intact. One experimenter, who reported on a number of cats transected at the midbrain or pontine level, believed that he could see the typical rage response in these animals (Keller). Others, however, felt that the complete rage response could be seen only when the hypothalamus is intact (Bard). Very recently there have been two sets of studies with the cat that give us a rather clear picture of the emotional patterns of midbrain and bulbar animals (Kelly *et al.*; Macht and Bard).

The first and most important conclusion is that only "subtotal responses" appear in such animals. They may growl, hiss or spit, lash their tails, thrash with their forelegs, protrude their paws, increase their breathing, urinate, and show various autonomic responses—nearly all the signs of rage in normal animals. These responses, however, are not always combined but may appear as isolated bits of behavior. Moreover, these animals never show the integrated "attack reaction" that one can see in normal animals, in which they attack with claws and teeth, directing their attack forward and downward and adopting the posture preparing for such an attack. Thus midbrain and bulbar animals, although they show some of the fragments of emotional response, do not show integrated rage behavior. That, as we shall see, is put together at a higher level in the brain.

A second feature of emotional behavior in midbrain and bulbar animals is that emotional reactions become more fragmentary with a lower brain-stem section. Cats with intact midbrain can right, stand, and walk, and they can give the items of emotional response that we listed in the paragraph above. With a section through the lower part of the midbrain or through the pons, animals no longer can right, stand, or walk. These animals also do not show so many of the items of rage response as do those with a somewhat higher section.

It looks, then, as though the various items of rage behavior have their 'seats' in the lower brain stem, that the lower we go in the brain stem the more likely we are to miss some of them, but that the organization of total emotional responses is carried out at a level above the midbrain.

The other side of the problem of the function of the lower centers is how the effectiveness of stimuli in midbrain and bulbar animals compares with normal and decorticate animals. There are apparently some changes on this score, but they are not always consistent from animal to animal and from species to species. One important point is that visual and auditory stimuli are ineffective in eliciting responses. This one might expect because their main centers are above the medulla and midbrain. The effective stimuli for the midbrain animal are somesthetic and nociceptive stimuli—pinching, electrical shocking, squeezing, and rubbing the animal. In some animals only painful stimuli are capable of provoking emotional responses; in others merely stroking or rubbing the animal brought forth growls or other emotional items (see Bard and Mountcastle).

THE HYPOTHALAMUS AND EMOTION

Almost any textbook of psychology nowadays will say that the seat of the emotions is in the hypothalamus. That statement is partly true, and it is based on the now classic experiments of Bard. As more and more experiments come to light, however, we find that the relation of the hypothalamus to emotion is not so simple. and a fairlv careful analysis of its role is required.

The Hypothalamic Preparation. The classic experiments that point up the importance of the hypothalamus were done with dogs and cats (Bard). The procedure was straightforward (see Fig. 127). In some animals the cerebral cortex was removed, while the thalamus and all lower structures were left intact. In other animals the thalamus as well as the cortex was sectioned, but the hypothalamus and midbrain structures were left alone. Finally, in other animals, the section of the brain stem was made below the hypothalamus or below the midbrain.

The emotional responses of the animals were studied before and after these various operations. There were several striking results. For one thing, the threshold for rage response was lowered after the removal of the cerebral cortex. In other words it was easier to get a rage response from an animal after decortication than before. Thus removal of the cortex apparently released some inhibiting or restraining influences of the cortex that keep subcortical rage mechanisms in check.

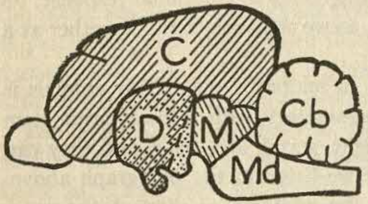

FIG. 127. Schematic longitudinal section of the cat's brain showing the different parts removed or left intact in studies of the neural basis of emotion. *C*, cerebral cortex; *D*, diencephalon; *M*, mesencephalon; *Md*, medulla; *Cb*, cerebellum. Cross-hatching from the right downward to the left indicates the portion of the brain that can be extirpated without interfering with the expression of rage. (*From W. B. Cannon. The mechanism of emotional disturbance of bodily function, p.* 879. *New Engl. J. Med.*, 1928, 198, 877–884. *By permission of the publishers.*)

Another fact was that the complete rage response could be elicited so long as the hypothalamus was intact. With sections below the hypothalamus, however, the emotional responses became fragmentary—they were the subtotal responses that we have already described for midbrain and bulbar animals. The rage response obtained in hypothalamic animals seemed just as complete as in normal animals. The conclusion, therefore, is that there is some mechanism in the hypothalamus for organizing the somatic patterns of emotional response. We also know, of course, that the main center for integrating patterns of autonomic effects is in the hypothalamus.

The statement that the hypothalamus can mediate complete patterns of rage must be qualified. Actually, the hypothalamic preparation has certain behavioral deficiencies that show up in emotion. It has, for example, some rigidity of the extensor muscles (see pages 305 to 308), such as is seen in decerebrate preparations. In general, too, hypothalamic animals lack some of the postural reactions that go along with full-fledged emotional response. On the whole, however, a relatively well-organized and integrated pattern of rage response can be obtained with the hypothalamus intact—and only so long as it is—in a series of decerebrations.

Hypothalamic Stimulation. There is other rather conclusive and somewhat more recent evidence that the hypothalamus is an integrating center for rage responses (see Ranson). It is possible to bury electrodes in the hypothalamus and to stimulate the region with electrical currents while an animal is unanesthetized or only lightly anesthetized. That has been done in a series of experiments. The result is that cats so stimulated behave as though they had come face to face with a barking dog. They give the full-fledged rage and attack response of the cat.

As well as we can tell, the only region in which we can stimulate electrically and get rage responses is the hypothalamus. They do not appear when the thalamus or other subcortical structures are stimulated. It has been possible to evoke rather coordinated facial and vocal responses from electrodes in the midbrain and pons, but these are more or less isolated responses. And the upshot of many experiments is that ". . . a fully integrated expression of anger . . . has never been produced by stimulation of any region of the brain except the hypothalamus" (Bard and Mountcastle).

Hypothalamic Lesions. With all this evidence before us, one would think that the hypothalamus is essential for the integration of the complete rage reaction. Just at this point, however, there is a hitch. There are experiments in cats and monkeys in which restricted lesions have been made in the hypothalamus (Ranson, Kelly *et al.*, see Bard and Mountcastle). Such animals, of course, are somnolent (see page 363), they are less active than normal, and their mechanisms for controlling body temperature are badly upset. And partly confirming our expectation, they show some definite, but not permanent, emotional stolidity, *i.e.*, they are somewhat less excitable than the normal animal. And their threshold for a rage response is higher than that of the hypothalamic animal. The striking fact, however, is that full, well-integrated and well-directed rage responses can be obtained in animals with restricted hypothalamic lesions. The appropriate sort of nociceptive stimuli will bring out such responses.

This, then, is the situation we face: If the higher structures of the cerebral cortex and thalamus are removed, we must have the hypothalamus in order to have a full-fledged emotional response. If we are electrically stimulating the brain, it is the hypothalamus that gives the well-integrated rage response upon stimulation. Finally, however, we can make restricted lesions in and around the hypothalamus, sufficient in size to damage all centers and tracts in the hypothalamus concerned with emotional behavior, and we still get complete rage responses.

This is a kind of situation we often meet in dealing with the nervous system. It means that there are alternative mechanisms for a particular pattern of response. In this case, experiments have not gone far enough to tell us just what the alternative mechanism is when the hypothalamus is damaged. One possibility, suggested by Bard and Mountcastle, is that the cerebral cortex can facilitate and integrate the emotional mechanisms of the midbrain and hindbrain. Put another way, the suggestion is that the cerebral cortex may, in part, take the place of the hypothalamus in making patterns out of the responses that are effected by the midbrain and hindbrain. Only further experiments can tell us whether this or some other possibility is correct.

THE CORTEX AND EMOTION

It was perfectly clear from Bard's classic experiments that some mechanisms in the cerebral cortex or forebrain normally restrain the hypothalamus. Only with such an assumption can we understand the greater reactivity of hypothalamic animals to giving rage reactions. In recent experiments we have been acquiring not only more information about the function of the forebrain as a whole but also something about the functions of some specific centers and pathways. Most of the data we have, however, concern rage responses, and when we say *emotion* in the paragraphs that follow, we are referring to the expression of rage. At the very end of this section we shall have a few words to say about fear and pleasure.

Decortication and Emotion

Although typical emotional responses can be obtained in hypothalamic animals lacking the thalamus and cortex, it is probably already clear from what we have said that the cortex plays a definite role in the threshold and pattern of emotional responses. In the experiments that physiologists have done on this matter, there have been two general approaches. One is to study the effects of complete decortication of an animal. The other is to study the effects of removals of restricted amounts of tissue of the cerebral cortex. We shall consider the results of both kinds of experiment. Here let us note the consequences of decortication (see Bard and Mountcastle).

Threshold. The first characteristic of emotional response in a decorticate dog or cat is a lower threshold. The animal is overreactive to slight pinches and pressures on different parts of the body. It will usually display a rage response at the very slightest provocation. Oftentimes any handling or stroking of the animal, even gently, brings out a full-fledged rage response. The picture, then, is one of increased sensitivity or lowered threshold for emotional stimuli. The obvious interpretation is that the cerebral cortex normally has some suppressing or restraining influences to exercise on lower centers and that these are removed when the cortex is removed.

Direction. Another, and a predictable, characteristic of emotional reactions in decorticate animals is lack of 'direction.' Although rage behavior is full-blown and well coordinated in decorticates, the animal seems to lack any appreciation of what it is that disturbs him. When, for example, the experimenter produces rage by pinching the decorticate dog's tail, the experimenter can feel quite safe from attack, for the dog's snapping and biting will be directed in front rather than to the rear where the painful stimulus is being applied. Of course, it is not hard to understand this aspect of decorticate behavior. The principal sensory mechanisms having to do with spatial orientation and perception of space are at the cortical level. Removal of the cortex deprives the animal of the basic perceptual equipment for making directed emotional attacks.

Timing. Another characteristic of decorticate emotional responses is their timing. When a normal animal is once excited by an emotional stimulus, it continues in an emotional state for some time. Not so the decorticate. Such an animal gets over its madness very quickly. In other words, normal animals show an after-discharge in emotional reactions that is considerably reduced in the decorticate animal. For example, an experimenter may pinch the tail of the decorticate dog and elicit rage behavior, but immediately afterward he may place his finger in the dog's mouth with little danger of being bitten—which is not nearly so safe in the case of a normal angry dog. We may conclude that the cerebral cortex has some braking and smoothing action with respect to emotion. It makes emotional responses a bit more difficult to elicit but once they are aroused contributes somewhat to their continuing for a time.

Anesthesia in Man. Confirming the notion that the cortex normally restrains subcortical centers for emotion are observations of the effects of certain general anesthetics in man. Some anesthetics, *e.g.*, ether, have differential effects on the nervous system. They attack higher centers before they affect lower ones. When such anesthetics are given to human beings, there is usually a period of excitement, restlessness, and thrashing about before deep narcosis sets in and the patient goes completely "to sleep." During this transition period, very striking emotional behavior is often observed. There may be weeping, groaning, laughing, or signs of rage. Comparable manifestations are sometimes seen in animals also. Such facts indicate that subcortical centers are normally under the control of the cortex.

Paralysis. There is a final point to be made from certain cases of patients with lesions of the cerebral cortex. As we have already seen, lesions in the precentral cortex, if they are severe enough and widespread enough, can cause paralysis. If these lesions are in the 'face areas' of the cortex, there may be a paralysis of the muscles ordinarily used in the expression of emotion. The interesting point is that such muscles, although paralyzed in 'voluntary' behavior, may come into play in genuine emotional behavior. This is important because it indicates that there is a complete mechanism for somatic patterns of emotion at subcortical centers, presumably the hypothalamus, without dependence upon the motor pathways originating in the cerebral cortex.

INHIBITORY STRUCTURES OF THE CEREBRAL CORTEX

It is only in the last few years that we have begun to get some idea of the specific structures of the cerebral cortex that take part in the restraining of hypothalamic and lower centers of emotion. We are still not exactly sure which areas are and are not important but we know the general regions of the brain that are important.

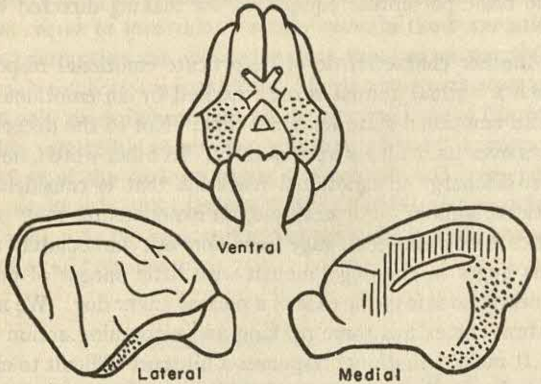

FIG. 128. The "emotional" areas of the cortex of the cat studied in the experiments of Bard and Mountcastle. The stippled area is the pyriform-amygdaloid-hippocampal complex, and the hatched area is the limbic and cingular gyri of the mid-line. On the left is a lateral view of the right cortex. In the center is a ventral view of the same hemisphere. On the right is a medial view of the cat's brain. (*After P. Bard and V. B. Mountcastle*, 1947.)

To explain what these regions are, we must go back for a minute to some distinctions that anatomists make about the brain. They divide the cerebral cortex into two parts. One is old and is found in the lower vertebrates; it is called rhinencephalon or sometimes allocortex. The other is phylogenetically rather new and is found almost exclusively in mammals; it is called the neocortex or pallium.

Allocortex. For many years anatomists have thought the rhinencephalon was a structure primarily of olfactory function, mainly because the olfactory nerves lead into the rhinencephalon. If you look at the ventral surface of the brain, you can see the olfactory bulbs, then the olfactory nerves leading backward to a vast complex of areas and pathways. These include the pyriform areas, the amygdaloid nucleus, and many other structures that we do not need to name. From them springs a structure called Ammon's formation or the hippocampus, which leads upward into the brain. Fibers from this formation end up by a complex route (see Fig. 128) in the anterior nuclei of the thalamus. This complex of centers and pathways may or may not have much to do with smell, as has been supposed, but it has a good deal to do with emotion, as we shall see in a moment.

Transitional Cortex. There are two other areas of the cortex often regarded as part of the neocortex, or cerebral cortex proper, which are nevertheless closely related to the rhinencephalon. One of these, sometimes called the transitional cortex of the mid-line, includes a number of areas lying deep within the longitudinal fissure just above the corpus callosum. There are several numbers and names attached to this general area. Let us, for brevity, speak of it simply as the *limbic* region (see Fig. 128). This area has two points of note. (1) It receives copious fibers from the anterior nuclei of the thalamus, thus connecting up with the rhinencephalic structures we have just considered. (2) The limbic region includes area 24, which we have seen earlier to be a cortical suppressor area (see page 295 and Fig. 118).

The Temporal Lobe. There is another area of cortex that we must mention in this connection, although it is still something of a mystery. It is the tip of the temporal pole. This, as you can see in most diagrams of the brain, juts down so that it is parallel with other ventral structures of the brain. The hippocampus and other structures of the rhinencephalon are, indeed, very close to it. The anatomical connections of the temporal pole have not been fully studied and are not too well known. There is reason to believe, however, that it is closely related to the rhinencephalon and to the transitional limbic cortex.

PLACIDITY AND FEROCITY

With this brief outline of the relevant neuroanatomy behind us, we can take up the question of what role these structures play in emotion. Most of the answer to this question comes from a very extensive study by Mountcastle and Bard with cats, following some preliminary observations of Spiegel and his colleagues (*cf.* Papez). These investigators made a variety of different operations in cats with three different results. Sometimes the cats became extremely placid, indeed, much more placid and peaceful than the normal cat. On the other hand, cats sometimes became extremely ferocious after certain operations, even more ferocious than hypothalamic animals ever are. And, of course, certain operations had little or no effect on emotional behavior. Which operations had which effects tells us a great deal about the cortical mechanisms of emotion.

Placidity. Cats are made placid—so placid that it is almost impossible to elicit a rage response in them—by removing a great deal of the cerebral cortex but leaving certain structures intact. The structures that must not be destroyed are the rhinencephalic centers and pathways that we described above—or more briefly, the amygdaloid complex—and the transitional cortex (limbic and cingular areas) of the mid-line. When all the rest of the neocortex is removed but these structures remain, cats are made into extremely peaceful, placid animals. Their rage responses are almost entirely suppressed.

This suppression of angry behavior with limited parts of the allocortex and transitional cortex remaining is in marked contrast to the reactivity of decorticate cats. These, we have just pointed out, are much more sensitive to emotional stimuli than are normal animals. We may come, then, to two conclusions. (1) It is perfectly clear that the amygdaloid complex and the transitional mid-line cortex are areas that suppress the rage-provoking mechanisms of the rest of the brain, particularly the hypothalamus. (2) The neocortex has some facilitating influence upon the rage mechanisms of the hypothalamus, for removal of the neocortex brings about placidity.

Ferocity. The experiments of Mountcastle and Bard carry the problem further and tell us some of the mechanisms for producing ferocity. Here, unfortunately, the facts become a bit complicated. They were able to convert a placid state into one of extreme ferocity by removing *either* the transitional cortex of the mid-line *or* the ventral amygdala complex, consisting of pyriform lobe, amygdala, and hippocampus. Just why the removal of either of these areas in addition to the removal of the neocortex makes the suppressing mechanisms fail, we do not know. But for some reason, both of them must be intact for placidity to prevail.

The experimenters went on to make restricted lesions of these "placid" areas without removing any neocortex. They did not observe any marked change when they took out only the transitional mid-line cortex. On the other hand, when they took out the amygdaloid complex and the pyriform lobe, they found that the threshold for provoking rage reactions was depressed. Animals could be much more easily aroused. They could be described as extremely ferocious. There is, however, a mystery about this effect—it does not make its appearance until several weeks after the operation. Whatever the reason for the delay, cats with such restricted lesions become quite ferocious.

It is interesting to note, too, that these ferocious cats had two points of advantage or difference over the sensitivity of hypothalamic animals to rage-provoking stimuli. For one thing, their attacks are much better directed than those of hypothalamic animals. The reason is easy to see: because their neocortex is intact, they can make use of visual, auditory, and kinesthetic cues in a much better way than the hypothalamic animal. A second and similarly explicable characteristic of the ferocious cats with restricted lesions of the allocortex is that their attacks are much better timed.

Interpretation. Research will continue in this field as in others and will gradually clear up many of the present questions and mysteries. It is possible, however, even at present to make a good deal of sense out of the facts that we have at hand.

In the first place, it is clear that a good deal of the ventral and medial part of the brain, long thought to be olfactory in function, has something to do with emotion. As well as we can understand the effects of different kinds of lesions, it looks as though the ventral allocortex is a "funnel" for inhibitory effects passing downward to the hypothalamus. The transitional cortex of the mid-line seems to contribute to these inhibitory effects, but the ventral allocortex seems to be somewhat more crucial (Mountcastle and Bard).

Not only are there suppressor effects of the cerebral cortex, there are also excitatory effects on emotion. When the "suppressor" areas are removed, animals are made much more ferocious than normal. They are indeed more ferocious and more skillful in their rage behavior than hypothalamic animals. Conversely, removing neocortex and leaving only allocortex and transitional mid-line cortex converts a cat into a placid animal. This result can only mean that the neocortex normally exerts influences that facilitate or help out rage emotional responses. Thus we can think of both suppressing and facilitating influences coming from different parts of the cerebral hemispheres to bear on the center for integrating rage reactions in the hypothalamus.

The Temporal Lobes. There are some rather confusing results of experiments involving the temporal lobes. We do not know just what to make of them, but we ought to report them briefly. It is possible to make monkeys very *placid*—monkeys that ordinarily are rather ferocious—by an operation somewhat similar to the one that makes cats *ferocious* (Klüver and Bucy). The operation in the monkey involves bilateral removal of the hippocampus, the uncus and amygdala, and the temporal lobes. The main difference between the two operations is in the additional removal of the temporal lobes. Whether this accounts for the difference in effects on emotion we cannot tell. In some preliminary experiments, it seems that removal of the temporal lobes of cats makes them placid just as it does monkeys, but it is too early to tell how these various findings fit together.

FEAR AND PLEASURE

Relatively little systematic research has been carried out on the neural mechanisms of fear and pleasure. These responses can be distinguished in various animals, at least in dogs, cats, monkeys, and people, but they are somewhat more difficult to produce at will, and that probably accounts for the paucity of data concerning them.

Fear. In some of his studies of emotional reactions in animals lacking cortex or forebrain, Bard has made a few observations of fearful behavior in cats. One of his tests was to blow a bugle or make the sound of escaping steam. In some animals there is a very marked response to such a sound. They scamper off toward walls and corners as though they were 'scared to death.' Such responses can be observed in totally decorticate animals. In fact, what evidence there is indicates that fear responses, like rage responses, are integrated at some subcortical level and probably in the hypothalamus.

Pleasure Responses. These are even more difficult to observe systematically than fear and rage. Purring in cats and tail wagging in dogs can be taken as signs of pleasure. Purring, however, sometimes seems to occur in cats when they appear to be angry. It is very dangerous to draw conclusions, but such evidence as we have would indicate that the pleasure mechanisms, or at least pleasure responses, are only found when some, or a goodly part, of the cerebral cortex is intact. It does not look as though they are subcortically mediated. At present, however, we are not sure.

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CHAPTER XVII

SLEEP AND ACTIVITY

We know from watching people and animals that they vary a lot in general activity. Sometimes they are moving about with great zest; sometimes they are resting quietly or even sleeping. On the face of it, these ups and downs of bodily activity look spontaneous—as though they "just happen." A little scientific study, however, tells us that so-called *spontaneous activity* is usually caused by specific changes in the internal and external environment of the organism. It is our purpose in this chapter to study these causes and how they control activity.

One of the most striking features of activity is its rhythm. Activity, in fact, usually follows several rhythms at once. One is the rhythm of sleeping and waking. Others are the rhythm connected with hunger and various drive mechanisms. In this chapter, therefore, we shall consider first the rhythm of activity we see in sleep and waking, and we shall come later to the matter of drives and activity.

PHYSIOLOGICAL CHARACTERISTICS OF SLEEP

Although we seldom make any mistake about whether a person or an animal is asleep, we have a hard time saying exactly what sleep is. For the moment, however, there are four main points to note about sleep: (1) it represents a low in bodily activity; (2) thresholds of various reflexes are increased in sleep; (3) in man, there is a loss of consciousness; and—to add a fourth criterion that separates sleep from some pathological states of drugs, comas, or head injuries—(4) the sleeping organism can always be aroused by strong sensory stimulation.

In considering the signs of sleep, we often find it hard to know what changes prepare the organism for sleep and what changes are the result of sleep. Many of the changes that we see will also occur, for example, if we simply lie down and stay quiet. On the other hand, relaxation and avoiding sensory stimuli are usually necessary for sleep. For the moment, let us avoid this difficult question of what is cause and effect in sleep and simply deal with the characteristics of sleep.

Somatic Activity. There are two conspicuous changes in reflex behavior that are signs of an organism going to sleep: (1) the muscles supporting the body relax and the organism usually lies down; (2) there is a marked tendency for the eyes to close. Both these somatic changes have been commonly taken as signs of sleep in animals. Both of them represent the elimination of major sources of afferent impulses that tend to keep the organism awake.

Once asleep, the organism remains relatively quiet, but it is obvious that somatic activity is not entirely absent during sleep. The surprising thing is how much an organism moves during sleep and how regularly bursts of activity alternate with periods of rest. In one study of human sleep, for example, the average period of uninterrupted rest was only about 11 min. In some individuals it was as low as 7 min. and in others as high as 25 min. (Johnson *et al.*). As you will see, the sleeping organism is constantly changing from light to deep sleep and is very often almost awake when it is asleep.

Autonomic Activity. In contrast to somatic activity, autonomic activity goes on whether we sleep or not. There are, however, some definite changes that take place during sleep and we can list them (see Kleitman). (1) Heart rate is significantly reduced, in some cases as much as 20 to 30 beats per minute. In general, however, it corresponds to the rate that we see under similar conditions of muscular relaxation during wakefulness. (2) Blood pressure also tends to go down in sleep. In one group of subjects, it was reduced 24 mm. Usually blood pressure reaches a minimum in about the fourth hour of sleep, rising somewhat thereafter, and comes up abruptly upon waking. (3) The volume of the brain increases, apparently as a result of the increase of blood in the arterioles. (4) Respiration is somewhat slower and its depth is greater than in waking, but the chief change is in its greater regularity. (5) Body temperature tends to drop slightly. In birds, for example, body temperature is lower during the normal sleeping time at night and higher during the day. When the light-dark cycle is artificially reversed, so are the times of sleep and wakefulness and fluctuations in body temperature. (6) Gastric contractions and alimentary activity go on as usual, if not with somewhat greater vigor. In general, all autonomic functions are about as one would expect when the organism is not engaged in activity and is no longer subject to the stresses of the world.

Reflex Excitability. In general, it is harder to elicit reflexes during sleep than in the waking state. This characteristic of sleep does not apply equally well to all reflexes, however. While the threshold for eliciting proprioceptive reflexes is heightened, the cutaneous reflexes are nearly normal. The knee jerk, for example, gradually disappears as a man goes to sleep. Cutaneous stimulation, on the other hand, seems to bring out rather normal response. Brushing the face produces a grimace, or tickling stimuli may elicit scratching movements. Of particular interest is the fact that the Babinski reflex may make its appearance in sleep. This reflex, a fanning of the toes, can be elicited in infants by scratching the sole of the foot. It never appears in the waking adult, however, unless there is neural injury that interferes with the flow of impulses through the pyramidal pathways from the precentral gyrus of the cortex. Apparently in the deeper stages of sleep this aspect of cortical activity is greatly depressed.

Electrical Activity of the Brain. More direct evidence that cortical activity is depressed in sleep comes from electrical studies of the brain. In fact, one of the most striking differences between sleep and wakefulness may be seen in electroencephalographic records (Fig. 129). (For a more complete discussion of electrical activity, see Chap. XXVI.) In going to sleep, the normal *alpha* waves (between 8 and 12 per second) disappear and are supplanted by a mixture of *spindle* waves (about 14 per second) and slow random *delta* waves (less than 8 per second, usually around 4 to 5), which are characteristic of deep sleep. Direct-current recording of cortical activity during sleep, furthermore, indicates that there is a decrease in the potential differences that exist between different points on the head compared to what is obtained in the waking state (King).

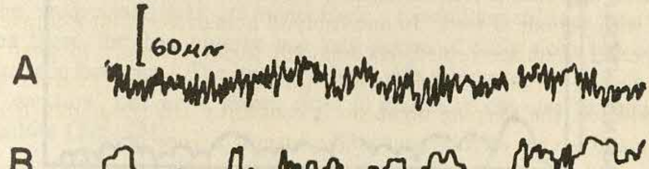

FIG. 129. The changes in the brain waves of a person going to sleep. *A*, alpha rhythm of wakefulness; *B*, alpha and delta waves of light sleep; *C*, delta rhythm of deep sleep early in the night; *D*, "null" rhythm which later replaces the delta rhythm; *E*, alpha rhythm on awakening. (*After N. Kleitman. Sleep and wakefulness. Chicago: University of Chicago Press,* 1939. *P.* 46. *By permission of the publishers.*)

The 'Depth' of Sleep. It should be obvious from most of these studies of the physiological characteristics of sleep that the depth of sleep varies during the night. We do not, however, go deeper and deeper into sleep, reach a maximum depth toward the middle of the night, and then gradually pass into light stages of sleep and wake up. This has been a common misinterpretation of the data on sleep. Most of the evidence agrees that the depth of sleep varies in a cyclical fashion throughout the sleep period. The individual passes from lighter to deeper stages of sleep and back again many times during the night. There are a number of ways to demonstrate this point, but one of the simplest is to measure the intensity of auditory stimulus necessary to wake the individual. At some points during the night the stimulus must be very strong; at others the individual is very nearly awake, judging from the weak stimulus that is needed to rouse him. The pattern varies from one individual to another and from one night to another in the same individual, but a typical record shows that sleep is a cyclical phenomenon (Fig. 130).

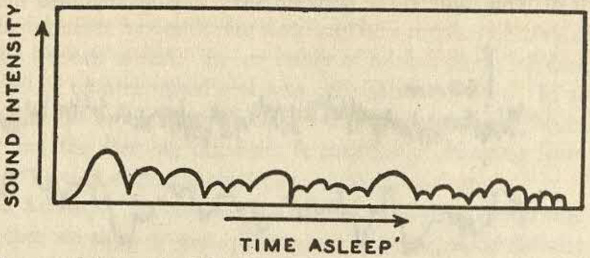

FIG. 130. Diagram of the way in which the depth of sleep varies throughout a night of sleep, as measured by the intensity of sound required to wake the individual. (*After N. Kleitman. Sleep and wakefulness. Chicago: University of Chicago Press,* 1939. *P.* 146. *By permission of the publishers.*)

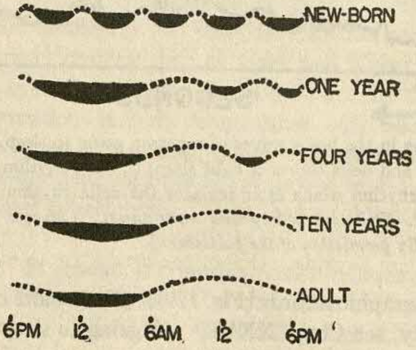

FIG. 131. Diagram illustrating the cycles of sleep and the change from polyphasic to monophasic sleep from birth to adulthood. (*After N. Kleitman. Sleep and wakefulness. Chicago: University of Chicago Press,* 1939. *P.* 515. *By permission of the publishers.*)

Sleep Rhythms. Aside from the variations in the depth of sleep that go on during any one sleep period, there are the wider fluctuations between sleep and actual wakefulness that make up the most conspicuous aspect of sleep rhythms. Now, different animals have different sleep and wakefulness cycles. Many animals, including man, sleep during one long period in every 24 hr. These are spoken of as *monophasic* animals. Many, on the other hand, display a number of alternate periods of sleep and wakefulness every 24 hr. Such animals are said to be *polyphasic*. Rats, rabbits, and in general, all rodents are polyphasic. Canaries, snakes, and man are monophasic. Several animals are intermediate between these, for they observe one long period of daily sleep but also take short naps in between. The human infant, it is interesting to note, is a polyphasic creature, but as it grows older it gradually changes to monophasic sleep habits (Fig. 131).

PHYSIOLOGICAL BASIS OF SLEEP

At the present time we do not have anything like a complete understanding of the physiological basis of sleep. A large number of studies have been done in this area, but clearly established facts are few. On the other hand there have been numerous theories, many of them speculative and most of them incomplete. Fundamentally, a theory of sleep must account for the rhythmic alternation of sleep and wakefulness. If it is to be a physiological theory, it must specify not only the organic changes that produce the states of sleep and wakefulness but also the mechanisms that permit these changes to operate periodically. So far, two kinds of physiological factors have been considered in the major theories of sleep: chemical and neural factors. As you will see, it is only for the purposes of discussion that we separate them, for both kinds of factors could operate at once.

Chemical Factors in Sleep

From time to time there have been several theories of sleep that ascribe it to chemical conditions in the internal environment of the organism.

Oxygen and Carbon Dioxide. One of the first of these was that sleep comes on because the horizontal position of the body and the demands of fatigued muscles call blood away from the brain and leave it without an adequate supply of oxygen. Such an *anoxemic* theory of sleep received a death blow, however, when it was shown in several studies that the brain of a sleeping person receives not less but more blood than usual.

It has also been argued that the waste products of metabolism so affect the brain that they bring on sleep. Most suspect of such products is *carbon dioxide*. This shows a significant increase in sleep, both in the amount that is expired in air and in that which is excreted. The trouble with believing carbon dioxide to be a cause of sleep, however, is that it increases after the onset of sleep rather than before. Furthermore, in animals and human beings forcibly kept awake for long periods of time, no change in the carbon dioxide tension of the blood has been observed.

Hypnotoxin. Another possibility is what Pieron called the *hypnotoxin* theory of sleep. According to this theory, it is supposed that there is some particular, though unidentified, substance produced in the blood and cerebrospinal fluid that leads to sleep. Supporting this belief are the early experiments of Pieron, in which cerebrospinal fluid was removed from a greatly fatigued animal and injected into the cerebral ventricles of a normal animal. Since the second animal became drowsy and fell asleep, Pieron concluded that the fluid of the tired animal must have contained a hypnotoxin.

Because this experiment left something to be desired in the way of adequate controls, it has been repeated by Schnedorf and Ivy. These workers found that they could reproduce Pieron's results by injecting fluid from a fatigued dog into a rested dog. Their control tests, however, showed that even when the fluid from a rested dog was injected into an animal, sleep could occasionally be produced. In fact, the same results were obtained when saline solution was injected into the cerebrospinal fluid and when the fluid of a rested animal was simply removed and reinjected. Since all these injections produced an increase in body temperature and in the pressure of cerebrospinal fluid, Schnedorf and Ivy concluded that (1) the sleep produced in their experiments was not 'normal' and (2) hypnotoxin may not be necessary for any of the effects observed. It is worth noting, however, that none of the control animals in this study slept as long or as deeply as many of the experimental ones that received fluid from a fatigued dog. More experiments are needed to tell whether this extra effect of fluid from fatigued dogs is a genuine one. If it is, then the chemical responsible for the effect must be isolated and identified. At this point, of course, Pieron's theory is neither proved nor disproved, for the experimental results are still equivocal.

Other chemical theories of sleep have been based upon more subtle changes that occur in the internal environment at the onset of sleep. On the belief that there normally is an increase in certain salts in the vicinity of the hypothalamus during sleep, one group of experimenters injected calcium chloride and other salts into the cerebral ventricles of cats (see Kleitman, page 291). In some of these cases sleep was actually induced, but control tests showed that any mechanical interference with the hypothalamus is likely to produce sleep (see below). Sleep has also been brought about by making human subjects drink large quantities of water and then injecting them with extracts from the anterior pituitary gland (Schütz). These procedures were calculated to produce the blood dilution and reduced urine output that are typical of sleep. In some cases sleep was produced by these procedures, but in others no real effects were observed. While many of these studies are highly suggestive, none of them have produced results consistent enough to give strong support for a chemical theory of sleep.

Against Chemical Theories. One of the strongest arguments that has been raised against any simple chemical theory of sleep comes from studies of Siamese twins. These twins have certain parts of the body in common and have, in the cases studied, interconnecting circulatory systems (Kleitman, page 483). In each of the three such instances available, one member of the pair may be very much awake while the other one is fast asleep. Similarly, in an experiment with two dogs in which cross circulation was established, inducing sleep in one animal by thrusting a needle into the hypothalamic region (see below) had no effect on the other animal (Neri *et al.*).

These experiments are not crucial evidence against a chemical theory of sleep, however. All they show is that, if there are any chemical factors important in the production of sleep, not enough of them reached the second organism. Obviously, much more work remains to be done before we can either accept or exclude a chemical theory of sleep. One point seems clear: even if chemical factors do play a role in the alternation of sleep and wakefulness, they are not the whole explanation. At best, they may play a contributory role along with other factors.

NEURAL MECHANISMS OF SLEEP

Most neural theories of sleep have supposed that there is a center for the regulation of sleep somewhere in the diencephalon of the brain, probably in the hypothalamus. The early clinical evidence seemed to bear out this view, for tumors and inflammations in the region of the hypothalamus were commonly associated with abnormal tendencies to sleep (somnolence). In many of these cases, however, the damage to the nervous system was extensive and usually involved parts of the thalamus and cortex as well as the hypothalamus. More precise information is now available from experiments on animals, where localized lesions have been produced in the regions of the thalamus and hypothalamus.

Experimental Somnolence. In his work with monkeys, Ranson has demonstrated that even with rather extensive bilateral destruction of the thalamus, there is no disturbance of normal sleep and wakefulness. On the other hand, if the lesions are restricted to the posterior part of the hypothalamus, in the region of the mammillary bodies and the lateral hypothalamus, profound somnolence results. Monkeys with such a lesion sleep almost continuously for 4 to 8 days after operation and show marked drowsiness for several months. At all times they can be roused by strong sensory stimulation, but they fall back to sleep again immediately. In the early stages of somnolence the animals cannot maintain normal body temperature and will not eat voluntarily even when roused. Furthermore, for several months after operation they are unusually passive emotionally. Lesions in the more anterior portions of the hypothalamus failed to produce somnolence or any of these other symptoms.

Because wakefulness seems to depend so crucially on the integrity of the posterior hypothalamus, Ranson designated this area the *waking center.* To account for its action, he assumed that the posterior hypothalamus exerts an excitatory effect upward on the cortex and thalamus and downward on the autonomic nervous system and spinal cord. Whenever the activity of the hypothalamus is high, he argued, the organism will be awake. If it is reduced, however, the activity of the rest of the nervous system will be low and sleep will result.

Essentially the same findings were obtained in a study of the rat (Nauta). Control lesions in subcortical nuclei other than those of the hypothalamus had no effect on sleep. Bilateral lesions in the immediate vicinity of the mammillary bodies, however, produced profound sleep from which animals could be aroused only by intense stimuli (Fig. 132). In addition, Nauta found that bilateral lesions immediately anterior to the mammillary bodies, particularly those involving the lateral hypothalamus, resulted in a state of drowsiness in which the animals were never fully awake nor fully asleep. Lesions that were more than 2 mm. anterior to the mammillary bodies, however, failed to produce any signs of somnolence. In this experiment, as in Ranson's, the somnolent animals could not maintain normal body temperature and would not eat. Many of them, in fact, developed respiratory infections and died within 2 weeks. But the fundamental disturbance in both these experiments was clearly the loss of the capacity to maintain wakefulness after destruction of the posterior hypothalamus.

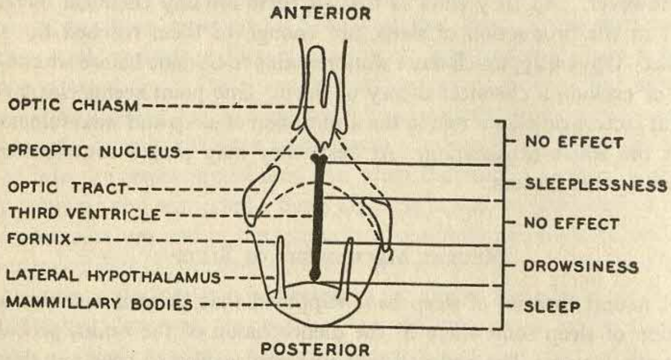

FIG. 132. Dorsal view of the hypothalamus of the rat, showing the regions where bilateral lesions produced states of sleep, drowsiness, and sleeplessness and where they had no effect on sleep. (*After W. J. H. Nauta. Hypothalamic regulation of sleep in rats: an experimental study, p.* 293. *J. Neurophysiol.*, 1946, 9, 285–316.)

Experimental Wakefulness. In another series of animals, Nauta found that bilateral lesions restricted to the region of the preoptic nucleus in the anterior hypothalamus made animals stay awake continuously. Upon recovering from the operation they were normally active, ate and drank voluntarily, and maintained normal body temperature. But they were never observed to sleep. After 24 hr. these rats began to show signs of fatigue. Their gait became unsteady and they would no longer eat or drink. In about three days they fell into a state of coma, from which they could not be roused, and died shortly thereafter. On the basis of these results, Nauta concluded that there must be a *sleep center* in the hypothalamus in addition to a 'waking center.'

If there is a center whose activity is essential for sleep, how does it exert its effects? In order to find out whether the 'sleep center' works by imposing inhibition on the cortex or merely by inhibiting the activity of the 'waking center,' a third series of rats was prepared. This time lesions were made both in the region of the mammillary bodies and in the preoptic nucleus. If the 'sleep center' has its effect on the cerebral cortex, the somnolence to be expected from the destruction of the 'waking center' should be abolished or decreased in this double operation. If, on the other hand, the 'sleep center' inhibits the 'waking center,' the net result should be no effect on somnolence. This is exactly what happened. Destroying both the mammillary bodies and the preoptic nucleus bilaterally produced the same degree of somnolence as lesions in the mammillary bodies alone. Therefore it was concluded that the 'sleep center' most likely exerts an inhibitory effect on the 'waking center.'

It is easy to see how the 'sleep center' could have been missed in other experiments. The critical area is small, and if the posterior part of the hypothalamus were also involved in any lesions, the somnolence that results would hide the existence of a separate 'sleep center.' Nevertheless it is surprising that in his careful work with monkeys, Ranson never reported sleeplessness as a consequence of hypothalamic lesions. In the clinical literature, however, a few cases have been reported in which severe insomnia preceded the onset of pathological somnolence caused by growths and inflammations of the hypothalamic areas. Since autopsy in these cases indicated that the lesions might have involved the anterior portions of the hypothalamus before the posterior region, some support is provided for Nauta's hypothesis. Such evidence is by no means conclusive, and, as Nauta points out, more experiments are needed on other animals, in addition to the rat, to confirm his findings.

Regulation of the Hypothalamus. For the present we may believe that there is both a 'waking center' and a 'sleep center' in the hypothalamus. The next question that comes up is how the two centers are controlled by other physiological factors. We have already discussed the possibility of chemical factors and were unable to establish clearly that such factors are causes either directly or indirectly of sleep. There is, however, ample evidence that other mechanisms in the nervous system, particularly other parts of the brain and incoming sensory impulses, have their effects in regulating the hypothalamic centers.

We may consider the *cerebral cortex* first. It has always been accorded an important role in sleep. In fact, Pavlov, the famous student of the conditioned reflex, believed that sleep was due to the irradiation of inhibition over the cortex. That we now know is not true, because dogs entirely deprived of their cerebral cortex are capable of sleep (Kleitman and Camille). Such decorticate dogs, however, do not stay awake for as many hours at a time as normal animals. The same sort of thing happens in people who suffer lesions of the cortical areas that are connected with the hypothalamus. They intermittently get more somnolent and drowsy (Davison and Demuth). Thus we know that the cortex is not essential for sleep or wakefulness but that it regulates in some way the activity of hypothalamic centers.

We must give some importance to the flow of *sensory impulses* into the nervous system. These certainly help activate the 'waking center.' We know, for example, that the cortex of a spinal animal shows brain waves that are characteristic of sleep and wakefulness. If, however, the brain of such an animal is sectioned above the level of the third nerve, only brain waves characteristic of sleep are obtained (Bremer). This means, presumably, that the sensory impulses coming in the first and second cranial nerves are not sufficient to keep the 'waking center' active. On the other hand, not very many sensory impulses are necessary for the activity of the 'waking center,' for the head end of a spinal animal will show alternations of sleep and wakefulness even though all impulses from the trunk and limbs are cut off in such a preparation. The upshot of this and other related evidence is that the 'waking center' is acted upon by other influences both cortical and sensory, but it probably functions in part as a self-exciting mechanism.

Problems. In general, the facts point to the hypothalamus as the center of the waking and sleep mechanisms and to other influences as secondary. There are, however, some problems and conflicts in the data that keep us from believing in any simple hypothalamic mechanism.

For one thing, we know that in some circumstances wakefulness can be imposed on an organism that has been deprived of its 'waking center.' It has been shown, for instance, that an animal made somnolent by lesions in the posterior hypothalamus can be aroused by strong sensory stimulation. Furthermore, Ranson has reported that monkeys with hypothalamic lesions become less and less somnolent with time. Apparently there are other centers that can function in maintaining the alternation of sleep and wakefulness. As a matter of fact, it has been reported that chronic decerebrate cats sleep and wake although they have been surgically deprived of hypothalamus and cortical regulating centers (Keller). It is possible that auxiliary centers exist in the brain stem which are not normally of great importance. One suggestion along these lines comes from clinical studies in which somnolence occurred as a result of lesions of the medulla (Davison and Demuth). It is also possible that sleep and wakefulness may be fundamentally a matter of the level of reactivity of whatever neural tissue remains in the organism. Of course, when the organization of the nervous system is nearly destroyed, it is meaningless to talk about sleep and wakefulness in the parts that remain. But sufficient organization remains in the decerebrate animal to refer to phases of inactivity and activity as sleep and wakefulness.

THE EVOLUTIONARY THEORY OF SLEEP

No one theory of sleep and wakefulness has been able so far to bring all these facts together in coherent form. Perhaps, however, the closest to being a complete theory of sleep and wakefulness in the intact organism is Kleitman's evolutionary theory. In this theory, he distinguishes two kinds of wakefulness: (1) a primitive *wakefulness of necessity*, which is the result of the activity of the 'waking center' and (2) a more highly evolved *wakefulness of choice*, which is dependent upon cortical function. Wakefulness of necessity is characterized by the polyphasic alternation of sleep and wakefulness seen in the decorticate dog, the newborn human, and many types of primitive animals. Whenever such an organism is relatively free from the barrage of afferent impulses arising from stimuli in the external world or its own muscular activity, the activity of the 'waking center' is reduced and it sleeps. But when stimuli arise from distention of the bladder, gastric contractions, or disturbances in the external world, the 'waking center' is excited and the organism is aroused from sleep. When it relaxes again and escapes external stimuli, the flow of afferent impulses is reduced. And so it goes in short alternating cycles of sleep and wakefulness.

In the animal with a more highly developed cortex, the alternation of sleep and wakefulness becomes a joint function of the hypothalamus and the cortex. Wakefulness of necessity is maintained by the hypothalamus, but superimposed on it is a wakefulness of choice maintained by the direct or indirect effects of cortical activity on the 'waking center.' Such cortical activity, Kleitman suggests, is largely determined by the learned and unlearned adjustments of the animal to the light-dark cycle of the world. In this way, sleep may be postponed and a monophasic rhythm of sleep and wakefulness may be developed in which the animal sleeps during the night and remains awake during the day.

Once the monophasic cycle is set up, in human individuals at least, it appears to become a bona fide rhythm of the cortex, 'waking center,' or both. In fact, the rhythm goes on whether or not the individual sleeps. In the extensive studies of prolonged wakefulness by Kleitman and his associates, they found that every aspect of the rhythm keeps up for considerable periods of time. Body temperature and activity, for example, drop at night and go up in the daytime. A subject is more awake, says Kleitman, on the third afternoon of prolonged wakefulness than he is on the second night. Thus the sleep mechanism possesses periodicity even when wakefulness is forcibly extended far over the normal period.

The evolutionary theory of sleep has the great merit of being general enough to encompass many of the known facts of sleep and to contradict very few. Although it stresses the roles of afferent impulses and the cortex in maintaining the rhythm of the 'waking center,' it does not exclude other possible factors that have been suggested. For example, if the existence of Nauta's 'sleep center' is confirmed, the evolutionary theory could take it into account as another factor that can determine the excitability of the 'waking center.' Similarly, the theory would have no particular difficulty in including any chemical factors that could excite or depress the 'waking center.'

ACTIVITY RHYTHMS

Turning now from sleep and waking, let us consider the gross activity of organisms without respect to whether they are asleep or awake when they are active. Activity, so conceived, has been measured by two general methods. The first makes use of the *stabilimeter*, a cage arranged on pivots or suspended by springs in such a way that any movement of an animal in the cage, even though exceedingly slight, can be registered by appropriate levers on a smoked or waxed paper (Richter). As ordinarily used, the stabilimeter gives records of the amplitude of movement, its frequency, and the time of occurrence. The second method employs a *circular cage* or floor, which moves, in the manner of a treadmill, with movement of the animal. From counting devices attached to the apparatus, the number of revolutions run by the animal in any given period of time may be determined, and this is taken as a measure of activity.

It should be pointed out that these two types of apparatus measure somewhat different aspects of bodily activity. The circular cage or revolving wheel records the *locomotor activity* of the animal, while the stabilimeter measures its *restless activity*. As you will see, this distinction is an important one, for experimental procedures that tend to weaken an animal may affect its locomotor activity but not its restlessness. And conversely, some procedures will increase restlessness but not locomotor activity.

Rhythms. One of the outstanding things about the activity recorded in these cages is the regular variation in the amount of activity an animal will display over a period of time. Some of these fluctuations may reflect the alternation of sleep and wakefulness, but there is more to the story than this. In fact, we know quite well what is at the basis of certain activity rhythms, and under the appropriate experimental conditions can alter and even entirely abolish some of them. Most of our information comes from studies of the rat. Analysis of the activity records of this animal shows that there may be several cycles superimposed on each other: short-run variations that occur every few hours, daily cycles, and cycles that repeat themselves every four or five days. As you will see, each cycle is attributable to a different environmental or physiological influence.

Hunger. Several experiments with rats and with human beings demonstrate the fact that bodily activity and hunger are closely related. Rats, if allowed to eat freely, display rather regular rhythms of activity and feeding, which occur, on the average, about every four hours (Richter). The activity almost always begins first, and only after it has continued for some minutes does eating take place; thereafter activity soon ceases. Similar findings, moreover, have been reported for human subjects studied while asleep, but in this case, instead of studying eating or verbal reports of hunger, records of stomach contractions were taken (Wada). Shifts of sleeping position and other more minor movements, it was found, preceded or attended episodes of gastric motility.

Having established this close connection of hunger or gastric contractions with bodily activity, one may ask which is the cause and which the result. One might be inclined to believe that the gastric contractions are the cause of the bodily activity, especially in view of the common belief that stomach contractions are the basis of hunger (see Chap. XVIII). In view of the fact, however, that in the rat activity *precedes* eating and in man bodily motility very frequently *precedes* gastric contractions, it is difficult to hold such a view. The preferable conclusion is that the two have a common origin in conditions influencing the nervous system. More extensive evidence for this conclusion is found in a later discussion of hunger.

Light. Under conditions of natural lighting, many animals show regular daily fluctuations in activity as the environment changes from light to dark. These cyclical variations are clearly seen in the rat, which is a nocturnal animal and displays about 70 per cent of its activity in the dark. Rats distribute their activity in the same way under artificial lighting schedules, even if these deviate widely from natural conditions. Browman, for example, has shown that rats will adjust equally well to 12-, 8-, and 6-hr. cycles of light and dark, always taking most of their activity in the dark. Furthermore, if the light-dark cycle is reversed, they will break away from their original rhythm and shift their peaks of activity to the new dark periods.

Once a diurnal rhythm is established, however, it is not always dependent upon fluctuations in light and darkness (Browman). Rats that are blinded or kept in constant darkness, after living under a regular light-dark schedule, will continue to show a diurnal rhythm. In some individuals the original rhythm will keep up for months; others will reverse their rhythms several times over a period of 2 or 3 months, but they will always maintain regular alternations of peaks and troughs of activity once every 24 hr. Similar results are obtained when rats are kept in continuous light, but the shifts in the daily peaks of activity occur much more frequently than in constant darkness.

Why rats adjust their activity rhythms to the alternation of light and dark is not entirely clear. It has been suggested that light, acting through the optic-hypothalamic-hypophyseal pathways, inhibits the pituitary gland. This gland, as we shall see below, is important in the regulation of activity. In experiments in which the pituitary gland was removed, however, rats continued to display normal diurnal variations in activity (Levinson *et al.*). They were able to reverse their rhythms when the light-dark cycle was reduced. All we know at the present time is that the retinas and optic nerves must be intact if activity is to vary with changes in the light-dark cycle.

Temperature. Although it has been shown that light is the most important factor in maintaining the daily fluctuation in activity, regular variations in environmental temperature may also play a role. By arranging a regular schedule of alternation of high and low temperatures, Browman was able to regulate the activity rhythms of blinded rats, *e.g.*, when the temperature of the experimental room was shifted from 16 to 27°C. every 6 hr., the blinded rats established and maintained 6-hr. activity rhythms. As you might expect, the peaks of the activity occurred during the cool periods. When normal rats are subjected to both temperature and light fluctuations, however, their peaks of activity occur in the dark whether or not it is also the cool period.

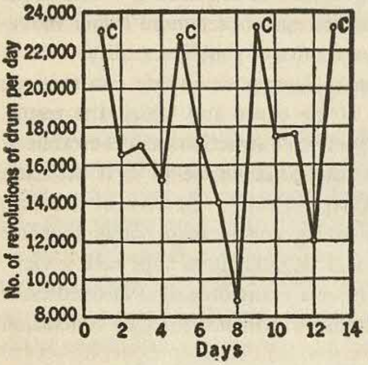

FIG. 133. Rhythms of gross bodily activity corresponding to estrual periods in the female rat. *C* next to a dot indicates that cornified epithelial cells were present in the vaginal smear and thus that the animal was "in heat." (*From G. H. Wang. The relation between "spontaneous" activity and estrous cycle in the white rat. Comp. Psychol. Monogr.*, 1923, 2, *No.* 6, *p.* 12. *By permission of Williams & Wilkins, publishers.*)

Sexual Drive. Gross bodily activity is also intimately related to sexual drive, at least in some of the infrahuman animals. In female sexual functions the relation is particularly striking. The female rat has a sexual cycle in which ovulation (page 423) and sexual receptivity occur rather regularly at 4- to 5-day intervals. Correlated with this cycle is a prominent rhythm of somatic activity, which shows up well in measurements of the number of turns run in a rotating drum (Wang; Brobeck *et al.*; Fig. 133). At the peak of the cycle a female rat may run as much as 10 miles a day, whereas on other days only a fraction of a mile will be run. The period of greatest activity, it has been shown by direct observations, corresponds to the time of "heat," or sexual receptivity. If at this time the female is copulated and made pregnant, no further periods of heat will be seen throughout the length of pregnancy (21 to 22 days); and throughout this period activity remains at a very low level. Thus it is clear that the activity is directly dependent upon conditions having to do with sexual receptivity.

Here, again, the question comes up as to what the cause of the activity is. This question is answered quite clearly in a section below dealing with the role of sexual hormones in activity. The gross bodily activity and the sexual receptivity both arise from hormonal conditions determined in the ovaries. As our later examination of the basis of sexual behavior will show, both probably are elicited by the direct effect on the brain of the hormones and the metabolic changes that they bring about, rather than by any sensory channels from particular organs of the body.

The male rat does not show the periodicity characteristic of the activity of the female rat but maintains, rather, a relatively constant level of activity. There is, moreover, little or no relation between the general activity of a male rat and the strength of its sexual drive as measured by the readiness with which it will avail itself of a receptive female (Stone and Barker). In this respect, therefore, there is no important relation between activity and strength of drive. Of interest also is the fact that reduction in sexual drive has no visible effect on activity, for animals allowed a period with a female rat in "heat" are just as active in a revolving drum as before.

NUTRITIONAL FACTORS IN ACTIVITY

As you might expect, the level of general bodily activity of an animal is related to its nutritional status. The relationship is not a simple one, however. Contrary to common expectations, not all kinds of deprivation lead to an increase in activity. Nor is activity a simple function of the degree of deprivation in all cases. Under some conditions of dietary deprivation activity does increase; but under others it may decrease, either immediately or after a brief increase. It is difficult to be certain why activity is affected differently by different kinds of deprivations. One general rule that seems to apply to many cases is that activity will increase as a result of deprivation, but only up to the point where the physical capacity of the animal is impaired.

Food and Water Deprivation. In a study of the effects of food and water deprivation on the rat, Wald and Jackson found that activity increased in rough proportion to the severity of the deprivation they employed. When rats were deprived of food alone, they showed an increase in running activity within the first day of measurement and continued to become more active as the deprivation progressed. After 5 days of complete deprivation, their activity was five times its normal level. At this point the experiment was terminated, and activity returned to normal levels in the first day of satiation. With 5 days of water deprivation, just about the same results were obtained. Total deprivation of food and water, however, led to a fivefold increase in activity in only 2 days. Apparently the effects of food and water deprivation are additive as far as activity measures are concerned.

Composition of the Diet. Even if animals are allowed food and water ad libitum, their gross bodily activity depends upon the composition of the diet that they are given. Smith and Conger maintained groups of rats on diets of equal caloric value but varied the content of fat and protein given to each group. When 50 per cent of the caloric value of the diet came from protein, activity was greatly depressed below the level of the control group, which was fed a balanced diet. Fat, on the other hand, could make up 56 per cent of the diet without reducing activity, and 75 per cent fat cut down activity only a little.

In other experiments, Richter and Rice maintained rats on diets consisting of a single food, carbohydrate, fat, or protein. In all cases, activity showed a brief increase above normal levels and then decreased slowly until the animal died. Of all the foods tested, carbohydrate diets permitted the longest survival and supported bodily activity at high levels. Such diets were even more effective when supplemented with thiamin. These various experiments tell us that marked imbalance in the proportions of carbohydrate, fat, and protein available to an animal will have a deleterious effect on activity. Animals made to depend primarily on protein are affected the most and those dependent on fat and carbohydrate the least, in that order.

Vitamin Deprivation. The effects of vitamin deficiency on activity are complicated, for different vitamin deficiencies lead to different effects. Rats that are maintained on thiamin-deficient diets show an increase in bodily activity for the first 10 days of the deprivation (Wald and Jackson). About that time the classic signs of polyneuritis appear and activity drops sharply below normal levels. A single injection of thiamin, however, restores the animal's physical condition and leads to an increase in food intake. During the period of increased food intake, activity may fall even further, but it returns to normal as soon as the excessive eating ceases.

Essentially the same results have been obtained in riboflavin deficiency and in deficiency of the entire vitamin B complex (Bloomfield and Tainter). On the other hand, when rats are deprived of vitamin A, of magnesium ions, or of total inorganic ions, there is no initial increase in activity. Rather it declines consistently from the very beginning of the deprivation. Vitamin D is also necessary for normal bodily activity. Richter and Rice have shown that rats maintained exclusively on diets of yellow corn fail to display normal activity until the diets are supplemented with vitamin D. Once the vitamin D is added, most animals attain their control levels of activity.

Conclusions. Two things, at least, should be clear from these experiments. (1) Increases in general bodily activity produced by dietary deprivation are probably not dependent upon stimulation from stomach contractions. It is unlikely that gastric activity becomes more severe over a period of 5 days of food deprivation. If anything, stomach contractions are apt to decrease in severity. Furthermore, the initial increase in activity in the cases of thiamin and riboflavin deficiency occur at a time when food intake is still normal. (2) The conditions that produce declines in bodily activity appear to be ones that weaken the animal physically. We do not know that this is true of every case, but we have direct evidence in the case of thiamin deficiency. In this instance it has been found that the physical endurance of rats, measured by their ability to keep swimming in a water tank, remains normal for about the first 10 to 15 days of deprivation. After that it declines sharply but may be restored by thiamin administration (Kniazuck and Molitor).

THE ENDOCRINE BASIS OF ACTIVITY

Because of the general importance of the endocrine organs in the physiology of the organism, numerous studies have been made of the role they play in the production of general bodily activity. In general, these studies show that the level of activity an animal can maintain depends crucially on the status of its endocrines. However, there has been some disagreement about the effects of removing particular glands and of administering hormones. Some of this difficulty arises from variations in the kinds of apparatus used to measure activity. But more often the trouble is in the interpretation of the physiological effects of extirpating endocrine glands and trying to replace their hormones later by injection. In considering the results of experimental studies, therefore, it is well to keep in mind that the endocrine imbalance produced by removing a gland may often be as important as the loss of the action of the particular glandular secretions themselves. Furthermore, as we have said elsewhere (page 96), replacement therapy by administration of hormones is at best incomplete.

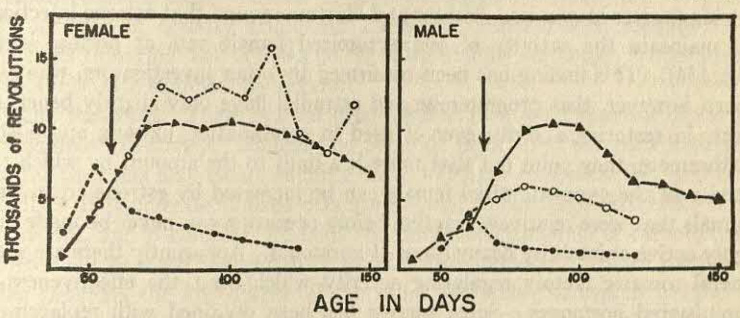

FIG. 134. Effect of amiotin (estrin) injection upon the activity of normal and gonadectomized rats. Triangles, uninjected normal rats; open circles, injected gonadectomized animals; closed circles, uninjected gonadectomized rats. (*After C. P. Richter and C. G. Hartman.*)

The Gonads. The ovaries, whose cyclical activities govern sexual receptivity in the female, are quite crucial determinants of activity. Using a revolving wheel apparatus, Richter finds that removing the ovaries reduces the activity of the rat to about one-fifth the normal level and completely eliminates all signs of cyclical functions as described above (Fig. 134). A similar reduction takes place in castrated male rats when their running activity is measured.

Whereas before operation there are marked individual differences in rats with respect to activity level and females show a higher level of activity than males, such differences are abolished by ovariectomy or castration. All animals seem to be reduced to a rather uniform, but very low, level of activity. It is interesting, however, that when the activity of male rats is measured in the stabilimeter type of cage, there is only about a 10 per cent reduction in activity following castration (Hunt and Schlosberg). Apparently the male hormones primarily affect the work capacity of the animal, so that marked deficiency shows up only when its running activity is measured.

Attempts at replacement therapy with gonadal hormones have met with varying degrees of success. Richter and Hartman found that estrone injections will maintain the activity of ovariectomized female rats at normal levels (Fig. 134). This finding has been confirmed by other investigators, who also report, however, that progesterone and estradiol have only slightly beneficial effects in restoring activity even if used in combination (Young and Fish). Furthermore, they point out that there is a limit to the amount by which the activity of the ovariectomized female can be increased by estrone treatment. Animals that were relatively inactive before operation can never be made into highly active animals by heavy doses of hormones. Apparently there are some general somatic factors regulating activity which limit the effectiveness of administered hormones. Some success has been obtained with replacement therapy in the case of castrated male rats, although complete restoration of normal activity is difficult. One interesting point is that estrone has a positive effect on male castrates, although the restoration of running activity is not so great as it is in the case of females (Fig. 134).

The Adrenal Glands. That activity is not entirely controlled by one particular hormone is indicated by the reduction in activity that follows extirpation of the adrenal glands. In fact, the reduction is quite marked, being on the average about 90 per cent. Apparently the cortex of the adrenal is responsible for this effect, for administration of cortical extracts reverses it. Increasing the quantity of salt fed to adrenalectomized animals, however, will produce a partial recovery of activity. Here again, it is likely that the lack of adrenal cortical hormone produces a physical weakness, which shows up as decline in activity. Supporting this view is the fact that the capacity to do muscular work depends directly upon adrenal cortical hormones (Ingle and Kuizenga).

The Thyroid Gland. Like other gland removals, thyroidectomy may lead to a reduction in activity. In cases where even tiny remnants of the gland are left intact, however, activity may be normal (Richter). More clear-cut results have been obtained with the use of thiouracil, which acts chemically to inhibit the production of thyroid hormone (Mann). When young rats are given as little as 0.1 per cent thiouracil solution in their food, they stop growing, show signs of reduced metabolism, and reduce their running activity within 10 days. Furthermore, estrous cycles and the regular variations seen in the activity of females are either abolished or disrupted. In general, the reduction in activity due to such procedures is not so great as when the adrenal glands or gonads are removed. Replacement therapy by feeding thyroid extracts is quite effective in restoring activity to normal, although administering too much thyroid hormone may lead to a further reduction.

Unfortunately, we know very little about the mechanism whereby the thyroid gland affects general activity. At one time it was thought that the lowered metabolic rate associated with thyroidectomy was responsible for the reduced capacity of the animal. However, it has been shown that dinitrophenol, which restores normal metabolic rate in thyroidectomized animals, fails to produce an increase in activity (Hall and Lindsay). Furthermore, feeding thyroid extracts to normal animals has no effect on activity, although it does increase metabolic rate significantly (Mann).

The Pancreas. There is some disagreement over what removal of the pancreas does to activity. Richter and Schmidt report that complete extirpation of the pancreas may create as much as 98 to 99 per cent reduction in total activity. If pancreatectomized rats are allowed to eat large quantities of proteins, fat, and B-complex vitamins and only small amounts of carbohydrates, there may be some restoration of activity (Richter *et al.*). Since this kind of diet prevents the appearance of the usual symptoms of insulin insufficiency seen in experimental diabetes, it would appear that the reduction in activity was, in part, the result of removing insulin from the internal environment. It has recently been reported, however, that taking out only 95 per cent of the pancreas leads to an increase in activity which can be reduced by insulin injection (Souto-Maior). The implication of this finding is that much of the reduction in activity Richter and Schmidt found following total pancreatectomy may be due to the destruction of nonendocrine pancreatic tissue. There is no resolving this dilemma in the light of present evidence.

The Pituitary Gland. Removing the pituitary body or cutting the stalk that connects it with the hypothalamus also causes a considerable reduction in the general activity level of rats (Richter). In this case the effects are to be explained, in part at least, by the influence of the pituitary gland on the growth and secretion of other glands. After removal of the pituitary, the adrenals, thyroid, and gonads show more or less atrophy, and these glands, as we have already stated, are all factors in activity.

Another point to be made concerning the effect of the removal of the pituitary is that the changes in activity include not only a reduction in its level but also, in females, a change in its rhythm. Whereas the normal female rat shows a 4- to 5-day activity cycle, the hypophysectomized rat tends to show a 14-day rhythm. To explain this finding, Richter offers the suggestion that the 14-day cycle is a multiple of the 4- to 5-day cycle and that it comes about because the amplitude of the changes in the ovary which are expressed in the 4- to 5-day rhythm is so reduced that it makes itself evident only, on the average, every three cycles. This hypothesis, Richter says, is upheld by the fact that in animals not showing the 14-day cycle there seemed to be a 9- or an 18-day rhythm, which would represent two or four normal ovarian cycles, respectively. The suggestion is not unreasonable, because it is known from other data that the ovary is normally stimulated by the hormones of the hypophysis (page 422).

THE NEURAL CONTROL OF ACTIVITY

It is apparent from the foregoing studies of the relation of hormonal and nutritional factors to activity that no one condition of the internal environment is responsible for gross bodily activity. As you have seen, many biochemical changes can produce increases or decreases in activity. But even with this knowledge, we are far from an understanding of the physiological mechanisms underlying activity until we can specify how the biochemical factors exert their effects.

Two lines of reasoning suggest that they act through the nervous system. In the first place, it is known that the activity of the nervous system is greatly influenced by changes in its internal environment of the sort we have been discussing. Secondly, it is reasonable to suppose that the production of bodily activity must be ultimately traced to the action of the nervous system. Therefore we shall turn to the question of what role the nervous system plays in the regulation of activity.

Subcortical Centers. We have already seen the profound disturbances in sleep and wakefulness that are produced by lesions in the hypothalamus. Such lesions, of course, do not afford us much information about waking activity, because they made the animals somnolent. There are two other experiments, however, in which lesions in the rat's hypothalamus caused a reduction in activity without any signs of somnolence. In one, the revolving wheel was used to measure activity, and it was found that damage to the ventromedial nucleus reduced running activity below preoperative and control-animal levels (Hetherington *et al.*). Similar but less marked results were obtained in a study of rats in which the stabilimeter type of cage as well as the revolving cage was used (Brooks). In both these experiments, many of the animals increased their food intake and became obese (see page 339). But the reduction in activity appeared whether or not obesity developed. Since such hypothalamic lesions impair the rat's ability to metabolize energy stores, it was suggested that both the decrease in activity and the increase in food intake were reflections of reduced metabolic capacity of the animals.

In an experiment on cats, lesions in the brain stem (interpeduncular nucleus) produced a change in the character of activity (Bailey and Davis). The animals developed what was called the syndrome of 'obstinate progression.' They kept walking forward until they bumped into an object, knocked it over, or fell down and got a new direction. In some cases this behavior continued to the point of exhaustion of the animals. Another report of essentially the same forward-going type of progression in cats was made by Mettler. This time the change in activity was produced by damage to the corpus striatum in the region of the tips of the caudate nucleus. Mettler suggests that the striatum normally inhibits the lower motor centers and that these are released from control when it is destroyed.

In the monkey, Richter and Hines noted a marked increase in activity following destruction of the tips of the striatum with minimal damage to the cortex. They measured the amount of activity objectively by chaining the animals to a rotating axle. In view of this method of measuring activity, it is not surprising that they did not mention any tendency toward forward progression. On the other hand, Beach made lesions in the striatum of rats and found no consistent effects. Of five animals, he found that only one showed an increase in running activity; two showed a decrease and two exhibited no change in activity after operation.

We have too little information at the present time to understand how subcortical centers operate in the control of general bodily activity. But we do know that they play a role in determining not only the amount of activity an animal will display but also the character of the activity. As you will see, some light is shed on these problems by the study of animals in which parts of the cerebral cortex, particularly the frontal cortex, have been removed. In these cases we again see an over-all increase in general activity as well as a change in the kind of activity displayed.

Frontal Cortex and Activity. The first suggestion that the frontal cortex was important in the control of general activity came from casual observation of operated animals that were being studied for other purposes (see Beach). In recent years, however, the problem has been investigated more thoroughly in a number of different animals and with quantitative as well as qualitative measures of activity. Unfortunately, the results of these experiments are somewhat complicated and will require detailed discussion.

The Rat. In their study of the rat, Richter and Hawkes came to the following conclusions: Removal of one frontal pole tends to increase the activity of all animals but affects less active rats more than more active ones. Upon removal of the other pole, thus making a bilateral operation, the increase in activity is very marked. The rats do not run themselves to death, but they come near to it. Along with the hyperactivity goes a greatly increased food intake and a considerable increase in irritability and savageness, the reasons for which are not known. Then, upon examining the sizes of the various endocrine glands in the hyperactive and normal rats, it was found that the pituitary glands of the operated rats were smaller and their ovaries larger than those of normal rats.

From these findings it was clear to Richter and Hawkes that removal of the frontal poles of the rat's cortex (possibly including some of the striatum) causes hyperactivity; but the reasons for the effect were not so clear. It might be that the crucial areas inhibit the growth and secretion of the gonads or of other glands and that when the areas are removed, the increased activity results from the greater production of hormones. The increased size of the ovaries in the operated animals supports this conclusion. The hypothesis, on the other hand, that the frontal areas inhibit nervous functions or that their removal makes the animal more distractible and thus more active is not ruled out.

The conclusions reached by Richter and Hawkes have to be modified somewhat by the later research of Beach. He found that lesions anywhere in the brain may either increase or decrease activity, although when in the frontal part of the brain they more often increase activity and do it in greater degree. Prominent in his findings is the same result that was met in the earlier more casual researches, that not all animals are made hyperactive by the frontal-area lesions. Beach, too, did not observe any increase in savageness in his animals. With such results considered it appears that, although the frontal areas have something to do with activity, further research is necessary to explain in what way and why the same results are not obtained in all animals.

The Cat. Experiments with the cat, carried out by Langworthy and Richter, appear to present very clear-cut results (see Fig. 135). Unilateral lesions lead on the average to a doubling of activity, and bilateral removal of the frontal pole results in a very remarkable increase in activity, on the average by a factor of *ten times*. Some animals may, indeed, run more than one hundred times as far per day as they did before operation, and as a consequence they may exhaust themselves and die. The hyperactivity is often accompanied by a ravenous appetite, but it is not known whether that is a direct consequence of frontal-pole removal or an indirect result of the hyperactivity; this, naturally, increases the demands of the body for energy.

Essentially the same results were found by Smith, who also noted, however, that the cats with frontal lesions showed a marked tendency to follow people or other moving objects blindly. He suggests that removing the frontal lobes may lead to a modification of inhibitory mechanisms in control of visual orientation and thus contribute to hyperactivity. Some support for this notion is found in a study of monkeys, where hyperactivity was abolished by blinding them, keeping them in the dark, or removing the visual cortex in addition to the frontal areas (Kennard *et al.*).

A survey of the work with rats and cats leaves no doubt that there is a genuine and dramatic increase in activity following removal of the frontal poles in these animals. For a more refined picture of what particular areas of the frontal lobes are responsible for these results, however, we must turn to experiments with monkeys, which have brains that are more highly organized and in which it is more possible and plausible to speak of specific areas than it is in lower animals.

The Monkey. All who have studied the problem in monkeys agree that hyperactivity, like other symptoms of frontal-lobe lesions, is much more pronounced in bilateral than in unilateral lesions; indeed, it is controversial whether the latter produce any significant effects whatsoever.

The results of Richter and Hines with objective means of recording activity indicate further that hyperactivity follows destruction of one particular part of the frontal area (Brodmann's area 9) more than that of any other, but that

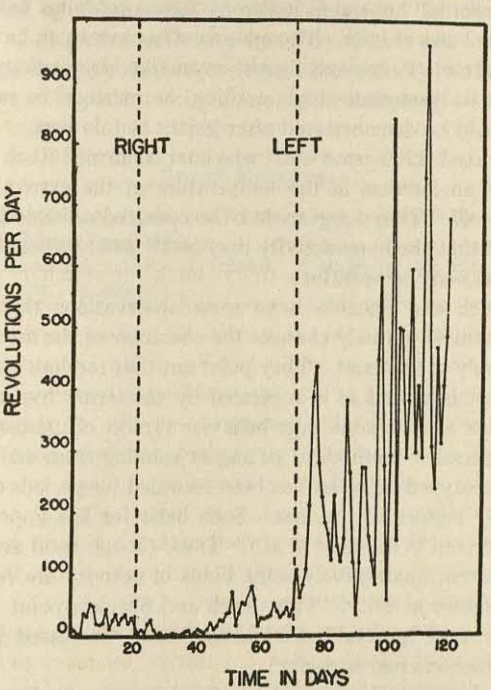

FIG. 135. Effect of removal of the prefrontal areas upon activity as seen in the record of a cat subjected first to right, then to left prefrontal lobectomy. (*After O. R. Langworthy and C. P. Richter.*)

the addition of a larger part of the frontal area (areas 10, 11, 12; see Fig. 113) will somewhat augment the effect. Kennard *et al.*, who also studied the question by objective methods, conclude that separate ablation of area 8, area 9, or areas 10, 11, 12 induces hyperactivity, but that all these areas must be removed to produce maximal hyperactivity. This study indicates equipotential rather than focal representation of the areas involved in activity.

Recently Ruch and Shenkin have shown that still another region, area 47 on the orbital or inferior surface of the frontal lobe, is of primary importance in activity. The region has been called area 13 by Walker, but it is labeled area 47 in Brodmann's system and that is the number we shall use here (see Fig. 113). Ablation of this small area produces hyperactivity which may be detectable on the first day after operation and which is well developed within a few days, after which it lasts permanently at a very high level. Because of the sheltered position of this area, it is probable that most of the other studies of removal of frontal areas and activity have not included this area. This, Ruch and Shenkin suggest, may well be a factor in the variability of occurrence, degree, and time of onset of hyperactivity from large prefrontal lesions that has characterized previous studies. Though area 47 is known to be related to the gastrointestinal tract (Bailey and Sweet), no marked hyperphagia (increase in hunger), increased gastrointestinal motility, or increase in rate of oxygen consumption could be demonstrated after lesions in this area.

On the other hand, Livingston *et al.*, who later confirmed Ruch and Shenkin's findings, report an increase in the temperature of the extremities following removal of area 47. They suggest that the operated animals lose body heat in this way and that the hyperactivity may result partly from the necessity to maintain normal body temperature.

However, Ruch and Shenkin have some observations that suggest that destruction of area 47 actually changes the character of the monkey's activity rather than simply the amount. They point out that random and spontaneous activities are not increased as is suggested by the term "hyperactivity," but that the complex and variable cage behavior typical of unoperated monkeys gives way to incessant methodical pacing or running from end to end of the cage. This stereotyped behavior has been recorded for periods of two or three hours with only momentary pauses. Such behavior has appropriately been described as "driven" (Kennard *et al.*). Thus, though total activity is quantitatively increased, qualitatively some kinds of activity are reduced and replaced by locomotor activity. This, Ruch and Shenkin point out, cannot be explained in terms of "generalized inhibition" or of "increased distractibility," as early experimenters had suggested.

A paradoxical result of lesions of the frontal areas, finally, is that hyperactivity may not appear until as late as 3 weeks after operation. And the stage of hyperactivity may be preceded by a period of considerably reduced activity, as measured by objective methods and by certain ill-defined behavior changes. Kennard *et al.*, for example, speak of the monkeys' appearing "confused, lethargic, slow, and difficult to arouse." Ruch and Shenkin note that fear and aggressive patterns of response are reduced and that the animals are unresponsive to environment and human presence. Acceleration of running is the main response to unusual stimuli. Particularly in animals subjected to removal of area 47, periods of complete immobility alternate with bouts of pacing that become progressively more rapid in rate and longer in duration. Thus the two types of symptoms, hyperactivity and apathy, coexist, especially in the first postoperative days. This fact leads one to believe that the prefrontal areas are not merely inhibitory in function but contribute in a much more complex manner to the patterning of behavior (Ruch and Shenkin).

From this brief review of the facts as they stand at present it is clear that a lesion of a phylogenetically new part of the cerebral cortex, the frontal "association" areas, can alter the level of behavioral activity both upward and downward. No defect of motion occurs and no pattern of reaction is permanently abolished, but the energy devoted to the characteristic locomotor pattern is greatly increased at the expense of other activities. Much remains to be learned about the significance and mechanism of this relation. Further research along this line may throw some light on disorders of activity and hyperactive states found in patients with neurological and psychiatric disorders.

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CHAPTER XVIII

BODILY NEEDS

The needs of the body, we have already seen, are important in general activity. Indeed, we may often use general activity as an index of a bodily need. Besides general activity, however, needs produce specific patterns of behavior that are useful in satisfying the needs. It is these specific patterns and the physiological mechanisms that regulate them that we are going to study in this chapter.

We have three main purposes in mind. The first is to find out what it is in the internal environment that causes the need or constitutes the need. The second is to see how the needs of the internal environment affect the nervous system to arouse motivated behavior. The third is to study how the nervous system works in regulating motivated behavior. We shall have each of these purposes in mind as we consider different needs. In some cases we do not know enough to answer all three questions about a particular need, but we shall do the best we can.

EVACUATION

Urination and defecation are reflex acts that human beings, and sometimes animals, learn to bring under voluntary control. These acts, however, often have complex patterns of behavior connected with them. Moreover, they are motivated in about the same sense that eating and drinking are. They therefore deserve our attention, at least briefly.

CHARACTERISTICS OF EVACUATIVE BEHAVIOR

Both urination and defecation are periodic. The stimulus for the acts is the accumulation of materials in the bladder and colon, respectively, and these build up over a period of time. At some point they reach a "threshold," which brings on the behavior that empties the cavities and starts the cycle over again. In rats, for example, urination is carried out rather regularly at two-hour intervals and defecation takes place about every five hours (Richter). During the quiet phase of the cycle the need builds up and in the other phase the behavior satisfies the need.

There is more to the behavior than that, however. There may be very elaborate preparations for the evacuation, and rather special stimulus situations may be required. Dogs and cats, for example, usually want a particular environment in which to evacuate. They must find dirt, sawdust, or a similar material for digging a hole, and they attempt afterward to cover their excrement. They also have characteristic stances that are different for the sexes.

Hormones and Urination. We have recently learned that hormones are responsible for the behavior pattern of urination in the dog. Normal adult males raise one leg when they urinate; normal females squat. Male dogs *castrated* in infancy, however, do not raise their legs when urinating (Berg). Yet if they are then injected with male sex hormones, the typical adult male pattern appears. Even spayed female dogs and female puppies treated with androgen from infancy on will show the male pattern of urination (Martins and Valle). Besides changing the pattern of urination in the female, moreover, the androgen apparently lowers the threshold of the response, for urination occurs in treated animals when the bladder is far less distended than in untreated animals. The androgen-treated female, furthermore, is more fussy about her environment and needs just the right environment before urinating, just as the normal male dog does.

There can be no mistake about these complex patterns of behavior being motivated. Beyond what we have said about hormones, however, rather little is yet known about the physiological basis of the reactions. All that we can add now is that the primary stimulus for the behavior arises in the accumulation of materials in the bladder and colon. From these organs, sensory fibers carry impulses to the central nervous system. The need in this case has its basis in a peripheral stimulus.

THIRST

Early psychologists and physiologists tended to think of thirst as a conscious experience. When they found the immediate conditions giving rise to the thirst experience, *viz.*, dryness of the mouth and throat, they were content. We know now, however, that thirst is more than a local sensation of dryness. It is a reflection of the organism's need for water, and as such, it depends on all the physiological changes that characterize the state of water need. We know a good deal about the changes that take place when an organism lacks water. The only problem is to find out how they work to regulate the drinking that the organism does. When we know when and why an organism drinks and how the amount it ingests is controlled, we will know the physiological basis of thirst.

Local Factors in Thirst. The most widely known theory of thirst, offered by Cannon and sometimes called the *local theory*, holds that thirst is the state of the mucous membranes of the tongue, mouth, and throat. According to this theory, thirst reflects the body's need for water because a lowering of the amount of water in the blood affects the saliva secreted into the mouth and throat. Going into details on this point, Cannon notes that the amount of water in the blood is held relatively constant from time to time even though water is needed, but that the constancy of water in the blood is maintained at a sacrifice of water in the tissues of the body. Since the salivary glands are part of these tissues, they are influenced by very slight changes in the blood. Thus dryness of the throat is a rather sensitive index of the body's need for water.

Local dryness of the mouth and throat may, as Cannon suggests, be the most prominent feature of the human experience of thirst. Yet the experimental evidence says clearly that local factors do not regulate water intake. They may serve to initiate drinking, but other factors are at work in regulating how much an organism will drink. Dogs, for example, whose salivary glands were tied off drank more than normal animals after they were left panting in a hot room for one to two hours (Gregersen and Cannon). When the daily water intake of such "dry-mouthed" dogs was recorded, however, they drank no more than normal animals (Gregersen). The same thing is true in other studies. By extirpating most of the salivary glands, Montgomery reduced the salivary secretion of dogs. Although the dogs drank more often, they drank normal amounts of water. Similarly, Steggerda reported the case of a man with congenital absence of the salivary glands, whose mouth was always dry. Like the dogs without salivary glands, he drank more frequently than normal people but never ingested excessive amounts in any one day. Finally, partial denervation of the throat and mouth, which presumably should reduce the flow of afferent impulses produced by local dryness, does not interfere with normal drinking (Bellows and van Wagenen).

Only when the dryness of the throat is directly related to general bodily dehydration does it seem to be related to the amount that an organism drinks. Holmes and Gregersen showed, for example, that the injection of hypertonic salt solutions into people makes them extremely thirsty and they drink excessive amounts of water immediately. Salivary secretion is virtually eliminated by such injections, and it usually is not restored to normal until about an hour after drinking takes place. Both the salt injection and the drinking, of course, produce bodily changes other than the decrease or increase in salivation. As you will see, these additional changes are the ones that are important in thirst, for they constitute the general need of the body for water.

THIRST AS A BODILY NEED

We have to think of thirst, then, in terms of the deficit of water in the body rather than as some local manifestation in the throat and mouth. Later we shall try to say just what a water deficit means in terms of the detailed physiology of the organism. At the moment it will be enough to explain how water deficits arise and how they regulate the water intake of the organism.

Water Balance. Without going into all details, we can point out some of the salient features of normal water balance in the mammalian organism. There are three important ways in which an animal can lose water: (1) by perspiration through the skin, (2) by evaporation of moisture in the respiratory passages, and (3) by the formation of urine and feces. Some of these ways of losing water are more important in one species than in another. The environmental conditions of heat and humidity and certain important changes in the internal environment also determine which way may be most important at any one time.

In contrast to the steady loss of water that can take place in these three ways, there is only one important way that mammals can restore water to their bodies. That is by drinking. Of physiological necessity, the amount of water taken in by drinking must match the amount lost. Drinking therefore must be regulated by the water deficit an animal piles up. This is true regardless of whether or not the deficit shows up in local dryness of the mouth and throat.

The Regulation of Drinking. The experiments of Adolph and his collaborators have given us a good idea of the mechanisms that regulate drinking. First of all, by careful measurement of normal drinking in animals, they have shown that these regulatory mechanisms are very sensitive to slight losses of body water (Robinson and Adolph). Dogs begin to drink, for example, when they have lost only 0.5 per cent of their body weight in water. When no food is allowed during these tests, they take water at frequent intervals, in amounts proportional to the water that they have lost. They do not, however, drink quite enough to make up their water losses completely unless they have access to food. If they can eat as well as drink, they take amounts of water that are proportional to both the amount of solid food ingested and their previous water losses. With food and water ad libitum, therefore, perfect water balance is maintained over long periods of time.

The same sort of accurate regulation of water intake is seen even more dramatically when dogs are deprived of water (Adolph, Bellows). In these experiments the water deficits were estimated by measuring the difference in body weight under conditions of free water intake and after deprivation. If the dogs were allowed to drink after various amounts of water deprivation, they showed an ability to 'estimate' very accurately their water deficits. The amount of water they ingested in a 5-min. period, in fact, was directly proportional to the amount of water deficit they had accumulated during the deprivation.

Experiments with Fistulas. More interesting information along these lines comes from similar experiments on dogs prepared with esophageal fistulas (Bellows). In these animals the esophagus was cut and the upper and lower ends of it were brought out to the surface so that the water they drank could not get to the stomach. In such sham drinking, just as in the normal drinking we described above, the dogs drank water in proportion to their deficit (Fig. 136). Carrying the experiment one step farther, the investigator placed water directly into the stomach through the opening in the lower part of the esophagus. After a period of deprivation, he put in the stomach an amount of water equal to the animals' water deficits. Then, after varying periods of time, they were allowed to drink. When they drank immediately after water had been placed in the stomach, they took enough to make up their water deficit just as if they had not been 'prewatered.' If drinking was delayed 10 min., they took some water but not enough to make up the deficit. After a wait of 15 min., moreover, the dogs did not drink at all. Similar results were also obtained in a normal animal given water through a stomach tube.

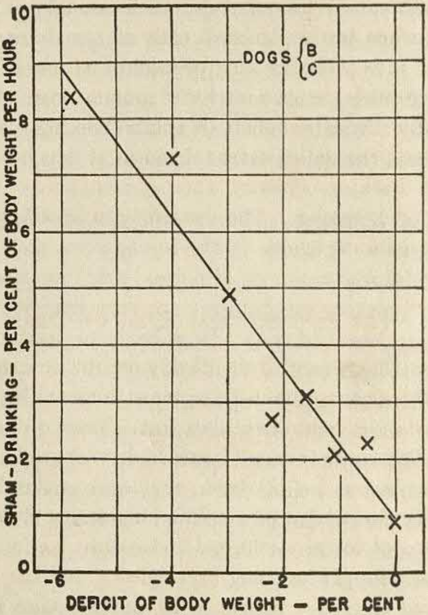

FIG. 136. Amounts of water ingested in sham drinking of fistulated dogs during steady deficits of water content. (*From E. F. Adolph. The internal environment and behavior: Water content, p.* 1372. *Amer. J. Psychiat.*, 1941, 97, 1365–1373. *By permission of the publishers.*)

These findings have been confirmed and extended in another study of dogs prepared with both esophageal and gastric fistulas (Holmes). In this case putting water directly in the stomach often did not inhibit drinking until it had been there for as long as 30 min. In addition, the experimenter let some of his animals, prepared only with gastric fistulas, drink normally. These animals completed their drinking, as normal dogs do, within about 5 min. At the end of this time, from 60 to 100 per cent of the water that they had drunk was drained from the stomach through the gastric fistula. Then the dogs were allowed access to water again. Within 5 min. they began to drink, but this time they took only small amounts and did not make up their water deficit for two or three hours.

Summary. Taken together, these findings let us come to some conclusions about thirst as a bodily need. (1) The amount of water deficit an animal incurs very precisely regulates water intake. (2) The amount of water in the stomach alone does not regulate drinking any more than local dryness of the throat does.

On the surface it looks as though water must have time to leave the stomach and reach the internal environment before drinking will be inhibited. This may be the case when water placed directly in the stomach inhibits drinking in 15 to 30 min. It is probably not the case in normal animals, however, for they stop drinking much too soon for water in the stomach to be the cause of it. We know, too, from the experiments on sham drinking that drinking does not depend on what happens to the water taken in. It is as if so much water deficit leads to so much drinking behavior whether or not a bodily need is satisfied. Ultimately, of course, the bodily need must be relieved by water. Otherwise the animals start drinking again.

THE PHYSIOLOGICAL BASIS OF THIRST

The conclusions that we get from these experiments, unfortunately, do not tell us what physiological mechanisms regulate thirst. They only give us a good general idea of what the thirst-regulating mechanism must be like. Ideally we need to know two more things: (1) what physiological conditions constitute the body need for water and (2) how they regulate the drinking behavior of the organism. We do not have complete answers to these questions, but we can point out some of the physiological factors involved in thirst.

Pituitary Hormones. It has long been known that the posterior portion of the pituitary gland secretes a hormone that is important in the normal water balance of the body (see Pickford). When this portion of the gland is damaged or removed, man and animals develop the symptoms of *diabetes insipidus*, *i.e.*, abnormally severe thirst (polydipsia) and excessive urination (polyuria). These two symptoms, we now know, can also be produced by damage to the supraoptic nucleus of the hypothalamus. This sends fibers to the pituitary and its stalk. In any case, the central factor in diabetes insipidus is a hormone put out by the pituitary gland and called the *antidiuretic hormone*. This normally inhibits the output of urine. Taking out the entire hypophysis, however, produces little or no disturbance in water balance. It has been supposed, therefore, that the anterior pituitary must normally secrete a *diuretic hormone*. In some cases, in fact, injecting extracts of the anterior pituitary causes polyuria and polydipsia, just as removing the posterior pituitary does (Richter).

To make a long story short, however, we can outline briefly the mechanism of diabetes insipidus, for we now know roughly what it is. The initial cause of it is lack of the antidiuretic hormone. Without this hormone, too much urine is excreted and lost, thus making the body deficient in water. The water deficit then causes the excessive thirst. That, in brief, is the mechanism as we have gotten it from experiments. Rats with lesions of the hypothalamic-hypophyseal system, for example, begin to lose water by urinating excessively shortly after they are operated on (Richter). The polydipsia, however, does not occur until one or two hours after the onset of polyurea. You can see these relations in Fig. 137.

What we have said does not rule out the pituitary gland as a direct factor in thirst. It may play a role. We know, for example, that more of the antidiuretic hormone that it puts out circulates in the blood when the body is dehydrated and needs to conserve water (see Pickford). Water deficit thus seems to affect the hormone, which in turn affects excretory activity of the kidney. Perhaps this hormone can also affect the nervous system and have something to do directly with thirst. We do not know.

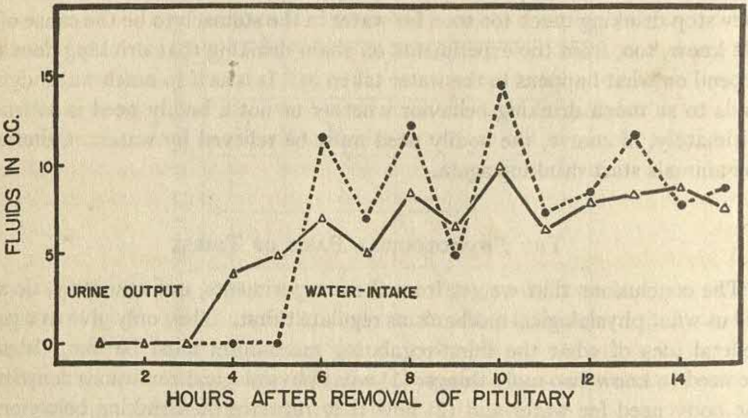

FIG. 137. Polyuria and polydipsia in the rat following removal of the posterior lobe of the pituitary body. Note that increased urine output (polyuria) precedes the increased water intake (polydipsia). (*After C. P. Richter. The internal environment and behavior: Internal secretions, p.* 880. *Amer. J. Psychiat.*, 1941, 97, 878–893.)

Changes in the Blood. Numerous experiments have tested the possibility that thirst is due to changes in the make-up of the blood. We know that the volume of plasma gets less and that the blood becomes more concentrated as water deprivation becomes severe. Yet other conditions that cause thirst do not produce these changes in the blood, *e.g.*, injecting hypertonic salt solutions causes thirst and also increases the plasma volume (Holmes). Conversely, in experiments with fistulas, salt injection causes a rise in serum concentrations of sodium and chloride even though drinking is inhibited by placing water in the stomach several minutes before. It may be that there are some crucial changes in the blood that can be tied up with thirst, but if so we do not yet know what they are.

Cellular Dehydration. There are many signs that the cells of the body are dehydrated in thirst. Gilman has demonstrated this point in a rather crucial experiment. He intravenously injected some dogs with a 20 per cent solution of sodium chloride and some others with a 40 per cent solution of urea. These solutions are isomolar so that they both produce the same rise in osmotic pressure of the blood. They penetrate the body cells at different rates, however. The saline diffuses into the cells slowly and as a result tends to draw water out of them very soon after the injection. Urea, on the other hand, is much more freely diffusible and permits equilibrium to be reached at the cell membranes without any loss of their water. The difference in drinking after these two injections is unmistakable. When water is allowed 15 min. after the saline injection, dogs drink large quantities. After urea injection, however, they do not drink until after an hour or more. It is then that they begin to lose water through the kidney in the process of excreting the excess urea. These findings have been confirmed by Holmes, who also found that sorbital, a carbohydrate that acts like hypertonic saline on the water in cells, causes immediate thirst.

It looks, too, as though the conditions that produce cellular hydration also inhibit drinking even when a water deficit has piled up. It is known that withdrawal of electrolytes from the extracellular fluid by intraperitoneal injection of 5 per cent glucose causes water to enter the body cells. Using this procedure, Darrow and Yannet observed that dogs that had been deprived of water would not drink even though the mucous membranes of their mouths were extremely dry. The state of hydration of the cells of the body therefore seems pivotal in thirst.

Theory of Thirst. We do not as yet have anything like a complete theory of thirst. Yet we know many of the physiological factors important in thirst and we have some idea of how the thirst-regulating mechanism works. First of all, it should be clear that many factors contribute to the regulation of water intake in thirst. Certainly local dryness of the throat and mouth is an important sign of thirst in humans. We have seen that it can serve to initiate drinking in animals as well as men. Yet it has little or nothing to do with how much an organism drinks.

The simplest statement we can make about amount of drinking is that it is proportional to the water deficit that builds up. Such a statement, of course, does not tell us anything about the physiological nature of water deficit or by what mechanism it controls the amount of drinking. We have fairly good evidence now, however, that cellular dehydration is the most important physiological condition in water deficit. Presumably this dehydration is general and involves the nervous system as well as the rest of the tissues of the body. We know, in fact, that dehydration has a direct effect on the supraoptic-posterior pituitary system, for the degree of cellular dehydration or hydration partly controls the secretion of the antidiuretic hormone.

It is conceivable that other effector mechanisms in the brain are similarly affected by dehydration and can regulate the amount of drinking an animal does. Or it may be that the diuretic hormone influences the central mechanism regulating drinking. Still a third possibility is that the neural centers that control the secretion of the antidiuretic hormone may also directly control drinking. We have no direct evidence to support any of these possibilities. Yet we know that other regulatory centers in the nervous system, such as the temperature-regulating center in the hypothalamus, function in the same way that we are supposing a thirst-regulating center might function.

HUNGER

As in the case of thirst, those who first worked on the problem of hunger had the conscious experience of hunger uppermost in their minds. Today, however, we recognize that the problem of hunger is one of the regulation of behavior. To know the physiological basis of hunger, we must know all the physiological factors that determine not only when and how much an animal eats but also what particular foods it selects. We can take up the first two problems here and leave the question of the selection of food for the last section of this chapter.

The Role of Gastric Contractions. About the oldest and most widely known of the experiments on hunger are those that concern contractions of the stomach. Cannon and Washburn did them. These physiologists used two methods to study gastric contractions: (1) x-ray observation of the behavior of the stomach for periods preceding, accompanying, and following the usual time of eating and (2) pneumographic recording of gastric motility from a balloon swallowed in the stomach. In each case they had subjects report every time they had a sensation of hunger. Both methods agreed in showing that when an individual reports hunger, gastric contractions are taking place. The experimenters therefore concluded that the conscious experience of hunger comes from sensory stimulation in the stomach.

Although that may be true, there are many facts that argue against the theory that gastric motility is essential to hunger. There are, first of all, cases of individuals without stomachs who give all the normal signs of hunger. In one such case, the stomach had been completely removed and the esophagus connected directly to the intestine. This patient ate normally and reported the normal desire for food (Wangensteen and Carlson). More crucial than this clinical case is an experiment conducted with rats whose stomachs had been experimentally removed (Tsang). These animals could learn a maze with food as the incentive just as quickly as could normal rats. They showed as much activity in connection with the time of feeding as normal animals. Finally, they got normal scores on the obstruction apparatus, which is often used to measure the strength of a drive. The principal difference between the operated and the normal animals was that the operated animals ate more frequently than the normal ones and could not stand 24-hr. deprivations so well. That is easy to understand, however, for animals without stomachs have no place to store very much food. The important point is that they had unmistakable signs of hunger in the absence of a stomach.

Other experiments have attacked the problem by surgically depriving the stomach of all nervous pathways to and from the brain. In two such experiments, rats with denervated stomachs displayed normal behavior with respect to food (Bash; Morgan and Morgan). They ate about as often as normal rats, showed the same activity changes in connection with feeding, and performed as well on the obstruction tests and maze learning when food was the incentive (Bash). The conclusion to be reached from all these studies is that neither the presence of the stomach nor nervous impulses from it are necessary physiological mechanisms in hunger.

CHEMICAL FACTORS IN HUNGER

The need for food is obvious. Not so obvious are the physiological conditions that make animals seek food and control their rate of eating. We know, of course, that depriving an animal of food causes many changes in its metabolism as well as in the functioning of many of its organ systems. It is not surprising, therefore, that a great deal of attention has been devoted to some of the biochemical changes that take place during food deprivation.

Blood-sugar Level. One of the first chemical factors suspected of playing a role in hunger was blood-sugar level. Early evidence indicated a tendency for the blood sugar to be lowered preceding periods of eating and to rise with satiation (Carlson). Later, however, it was shown quite clearly that there was no significant correlation between normal fluctuations of blood sugar and the onset of periods of activity and of hunger (Scott *et al.*). Yet it is also certain that the injection of sugar may inhibit stomach contractions and that insulin injections, which lower blood-sugar level, increase them. Closely related is the fact that insulin serves to increase the rate of eating in both rats and men (Morgan and Morgan, Freyburg). Furthermore, the effect of insulin on hunger in man is quite independent of nervous impulses arising from gastric contractions, since it shows up after vagotomy (Grossman and Stein). Similarly, in rats and dogs the vagus nerves may be cut and the increase in eating rate due to insulin will be even greater than before (Grossman, Cummins, and Ivy).

Hunger Hormone? Aside from these effects of insulin on hunger, we know that the blood of hungry animals is different from that of satiated animals. We do not know exactly how it differs, but it does. Transfusing the blood from a starving to a satiated dog will produce stomach contractions in the satiated animal (Luckhardt and Carlson). Also, transferring the blood from a recently fed animal to a starved animal inhibits stomach contractions (see Bash). Apparently there are different chemical factors that appear in the blood during satiation and hunger.

There is also reason to believe that the chemical factor connected with hunger is secreted from the stomach and therefore may be a sort of hormone. In one kind of experiment, parts of the stomach or intestines of dogs were cut away, severed from all nerves, and transplanted with intact blood supply as a pouch in the skin. The transplanted pouch contracted normally and secreted gastric juices along with the innervated stomach (Templeton and Quigley). Also, when food or sugar was taken into the stomach, contractions in the pouch stopped. Since injecting sugar into the blood stream had no effect on the activity of the pouch, it was concluded that the stomach or intestine must secrete chemical substances when stimulated mechanically or chemically.

So far the 'hunger hormones' have not been identified. They apparently can excite or inhibit stomach contractions, but we do not know whether they will bring on eating behavior. It is quite possible, of course, that these hormones can affect the central nervous system just as they affect the stomach. Indeed, we have suggestive evidence that other chemicals can influence both the stomach and the central nervous system. At least, we know they can affect the rate of eating quite aside from their influences on gastric contractions. Insulin, for example, will increase the rate of eating of rats with *vagotomized* stomachs, although such denervation keeps insulin from affecting gastric contractions (Morgan and Morgan). Conversely, *d*-amphetamine depresses eating even when the stomach is denervated and the drug consequently does not inhibit gastric contractions (Sangster, Grossman, and Ivy). Both these findings imply that hunger can be aroused or depressed centrally by the excitation and inhibition of parts of the central nervous system.

THE NEURAL CONTROL OF HUNGER

Whatever the particular tissue changes may be that are important in hunger, they obviously must influence eating behavior through the nervous system. Indeed, from what we have just said, it looks as though they act directly on the central nervous system. Just where they act we do not yet know. We do know something, however, about the centers and pathways of the nervous system that are involved in the control of hunger.

The Hypothalamus. Ever since the development of accurate instruments for reaching centers deep in the brain, it has been known that electrical stimulation of the hypothalamus will induce changes in gastric motility (see Fulton). A stimulus in the medial parts, *i.e.*, in the region of the tuber, increases stomach contractions. If the vagus nerves are cut, such a stimulus has no effect. On the other hand, stimulation of the posterior hypothalamus inhibits gastric contractions, *Hyperphagia.* More recently we have learned that bilateral lesions in the region of the ventromedial nucleus of the hypothalamus enormously exaggerates the eating behavior of experimental animals (Brobeck; Brooks). The change in behavior after operation, called *hypothalamic hyperphagia* (overeating), develops in three rather distinct phases. (1) Just after the operation, even before the animal fully recovers from anesthesia, it ravenously attacks food and eats large quantities of it. (2) After about 24 hr., the animal settles down to a steady eating schedule. In any 24-hr. period, it eats two to three times as much food as a paired control of the same age, sex, and initial weight. This period of increased food intake, known as the dynamic phase, continues for 1½ to 2 months, during which time the animal may double its weight. (3) The animal finally reaches a peak weight and does not get any heavier. At that point it cuts down its food intake to more nearly normal levels, but it still maintains its excess weight. This period is known as the static phase.

Hyperphagia appears to be the primary consequence of the hypothalamic lesions. The obesity is secondary to the overeating, and many of the other deviant symptoms these animals show can be attributed to their great weight and voracious eating habits. In addition, however, hyperphagic animals may show some symptoms that go along with damage to areas outside the ventromedial nucleus of the hypothalamus. In some cases operated animals become highly emotional, others may develop somnolence, and still others show a reduction in general body activity. None of these changes are essential to the appearance of the hyperphagia and obesity.

Characteristics of Hyperphagia. Investigators have studied hypothalamic hyperphagia in a number of different animals, but they have gotten the most detailed information about the rat. The following interesting facts about hyperphagic animals have been noted by Brobeck and Brooks and their collaborators. (1) They have the same basal metabolic rate as normal rats. (2) After a meal or the injection of glucose they show an abnormally large rise in respiratory quotient, often yielding values greater than unity. This extreme rise in metabolic rate seems to be a consequence of hyperphagia rather than a cause of it. It does not appear in operated animals until after they have been overeating for several days, and it can be produced in unoperated animals by making them eat their daily quota of food rapidly in short daily feeding periods. (3) Not only do hyperphagic rats eat faster than unoperated animals, but they spend more time eating. (4) Surgically reducing the size of the stomach does not abolish overeating. Neither does vagotomy appear to interfere with hyperphagia, but too few animals have been studied to be certain on this point. (5) Given a chance to select fat, carbohydrate, and protein from separate food dishes, the hyperphagic animals take the same proportions of each as normal animals do. (6) Animals cease to overeat when they reach maximum obesity, but they can be made hyperphagic again after their weight is reduced by brief periods of starvation. (7) Autopsy of hyperphagic animals reveals nothing of note beyond enlarged alimentary tracts, hypertrophied gonads, and enormous deposits of fat under the skin and around the viscera.

From these findings it is clear that the hypothalamus contains a center for the regulation of food intake. Both Brobeck and Brooks believe that this center functions primarily to maintain the balance between energy output and food intake. When it is removed, the balance is destroyed and the energy demands of the organism no longer control food intake. We have no direct evidence yet to indicate what physiological influences normally control this regulatory center. It may be that some of the chemical factors important in hunger exercise an effect on its activity, or neural impulses arising from the stomach or the cortex may play some role.

Frontal Cortex. As you may remember, hyperphagia has also been reported in a few of the experiments concerning the frontal cortex and general hyperactivity (Richter and Hawkes, Langworthy and Richter). Not all the studies reporting hyperactivity after frontal operation also report hyperphagia, but there is reason to believe that the frontal cortex may have some control over food intake. We know, for example, that electrical stimulation of many points on the frontal cortex causes increased gastric contractions and that stimulation of area 47 inhibits gastric motility (see Fulton). Ablation of the frontal cortex, furthermore, sometimes leads to hyperactivity of the gastrointestinal tract and spasms of the stomach, which may last for several days after operation. We do not know whether there is any relation between cortical and hypothalamic hyperphagia, but we can strongly suspect it in the light of what we know about the interactions possible between these two centers.

SPECIFIC HUNGERS

The problem of hunger is complicated by the fact that there are not one but many hungers. Not only does the organism regulate when, how much, and how fast it eats, but it also selects what it eats. As a general rule we can say that if an animal needs a particular food substance because of a metabolic disorder or because that food has been excluded from its diet, it will develop a *specific hunger* for the food. There are some apparent exceptions to this generalization, which we can take up later. Yet in cases where specific hungers show up clearly, we can demonstrate three things: (1) the organism will prefer the food it needs to other foods that are available; (2) it will usually ingest large enough amounts to meet its specific physiological requirements; and (3) it will eat the needed food even when its stomach is full. Obviously, this aspect of the regulation of food intake does not depend upon stomach contractions. In fact, the mere existence of specific hungers is the best evidence that gastric conditions are neither the chief nor the sole sources of hunger. Obviously there must be other biochemical and nervous mechanisms, and we shall look into them.

Self-selection of Diets. One of the best signs that there are specific hungers apart from general hunger is the ability of organisms to select a balanced diet from an assortment of all the necessary components of a good diet. Human adults probably would have difficulty selecting foods that are good for them on the basis of specific hungers, for they have developed food habits that could easily obscure any natural preferences. Young children, on the other hand, show the capacity to select food according to their body needs, if they are offered all the component foods they require (Davis). On any one day they may eat large quantities of butter or meat, for example, just as if they had an overwhelming hunger for some essential material in these foods. Over a long period of time, however, their preferences shift from one kind of food to another so that they achieve a balanced diet and grow normally.

A similar situation obtains in rats (Richter). If these animals are presented with several dishes of food, in each of which is one element—*e.g.*, salt, sugar, or fat—that is necessary for the normal functioning of the body, they will eat from each dish an amount which is just about correct for their needs.

The rats, furthermore, showed a remarkable capacity to adjust their caloric intake to their needs. When they were given extra calories in their drinking water in the form of sugar or alcohol, they cut down the caloric values they took from solid foods (Hausmann). The same sort of thing occurred in mice exposed to cold and warm environmental temperatures. Self-selection tests show, furthermore, that the increase in their caloric intake in the cold was due mainly to the large amounts of carbohydrate they ate and their decrease in the warm was made by cutting down their carbohydrate intake. Under both conditions, fat and protein intake remained essentially unchanged (Donhoffer and Vonatzky).

Factors in Self-selection. The self-selection feeding method works so well under some conditions that rats that obtain all their food in this way may actually grow more rapidly than animals maintained on standard laboratory food mixtures (Richter). Not all animals make beneficial selections equally well, however. There are wide individual differences and perhaps even strain and species differences. In two different studies of rats, for example, about one-third of them failed to grow normally when allowed to select their own diets (Pilgrim and Patton; Scott).

These studies suggest a number of different factors that are important in determining whether or not rats make beneficial food selections. For one thing, the age at which the animals are tested makes a difference. In Pilgrim and Patton's study, rats that failed to grow adequately on self-selection diets at the age of one and one-half months grew normally when tested 3 months later in the same situation. Also, the rats that did poorly on self-selection invariably failed to take adequate amounts of protein (casein) and often obtained more of their calories from fats than from carbohydrates. Furthermore, the rats that selected poor diets were the animals that grew the slowest when fed a stock diet mixed from the same components used in the selection tests. Finally, we have learned that different animals prefer different kinds of fats, proteins, and carbohydrates (Scott and Quint; Scott and Verney). In a study of protein, for example, animals that would not eat casein readily took fibrin or lactalbumen as their protein source and grew normally.

These individual differences in food preferences and the inability of some animals to make beneficial selections raise fundamental questions concerning the basis of specific hungers. It may be, for example, that the preferences of particular animals are merely reflections of special metabolic needs. One could argue that some rats fail to grow normally on both self-selection and stock diets because they require certain kinds of food that are not offered in the laboratory situation. On the other hand, it is likely that rats can learn strong preferences and aversions on the basis of the taste, smell, or consistency of foods, with the result that their natural preferences are obscured (Scott). A third possibility, and an important one, is that certain animals may be unable to taste particular kinds of foods and therefore will be unable to find and select them. Or conversely, certain purified foods may not have distinctive enough taste, smell, or consistency to be detected by animals.

Actually, it turns out that all these factors operate in the regulation of food preferences and selections. We can get some idea of their relative importance by considering experiments concerned with (1) the nature of food preferences, (2) the importance of body needs in the development of specific hungers, and (3) the role of stimulus characteristics of food in the detection and selection of foods.

Food Preferences. While the method of self-selection may indicate what foods an animal needs, it does not tell us very much about the nature of food preferences. Other methods of observation and measurement are needed. One such method is to confront an animal with two containers of food and allow it to start eating from either one (Young). If this procedure is repeated a number of times, the animal selects or prefers one food more than the other. In this kind of situation, rats prefer sugar to casein. If they are deprived of casein and allowed ample supplies of sugar before being tested, however, they prefer the casein. In general, as long as two foods are distinguishable, we can accept a general rule that an animal will show a preference for the one of which it has been deprived.

Unfortunately, the situation is not always so simple. Rats that have come consistently to select sugar under the influence of a sugar need may continue to prefer sugar at a later time when their need is for casein (Young and Chaplin). Only after a long series of trials do they shift their preferences to the casein. This apparent violation of the general rule just stated is easily explained, however. An animal prefers foods that it needs, but preference behavior becomes a habit, which may persist when the animal is tested in the same situation but with a different need. If the animal is tested in an entirely different physical situation when the shift in body need is made, it shows a preference for the food it needs and not the one it learned to select in the old situation. In fact, if the animal is tested in both the old and the new situation on alternate trials, it shows a preference for sugar in the old and a preference for casein in the new situation. The habits animals develop obviously can easily obscure their 'true' bodily needs. That bodily needs are important in specific hungers we shall see even more clearly in the next sections.

Pregnancy and Lactation. One of the best signs that specific hungers actually do vary with the bodily needs of the organism comes from the study of pregnant rats. During pregnancy, because of the demands of the growing fetuses, the mother's need of many minerals, particularly sodium, phosphorus, and calcium, is greatly increased. For the same reason she needs more fats and proteins. Sugar, however, is of no more importance than usual and may, in fact, be less necessary because the mother tends to expend less energy in muscular activity and maintains a somewhat lower metabolic rate.

All these changes in the physiological requirements of the body during pregnancy are reflected in this period in shifts of preferences for foods. Specific hungers for minerals are much stronger; those for fat and protein are also raised; but the intake of sugar is lower. The same general conclusion applies to the mother's preferences during the nursing period following birth, for the task required of the mother is much the same as in pregnancy. After the young rats are weaned and the physiological demands move back to normal, so also do the hungers for specific dietary materials.

Endocrine Factors. We can also see in endocrine disturbances the importance of the internal environment in arousing specific hungers. If the pancreas is removed, for example, a rat kept on stock diet develops all the symptoms of diabetes. When allowed to select their own diets, however, pancreatectomized rats do not show diabetic symptoms (Richter *et al.*). As you can see in Fig. 138, the reason for this difference apparently is that diabetic rats take very little sugar and make up for lost calories by increasing their intake of fat (Richter and Schmidt). As you will remember, the opposite kind of change in food selection takes place under low environmental temperature, which increases the metabolic rate. Apparently for the same reasons, increased carbohydrate intake can be brought on by injecting thyroxine (Donhoffer and Vonatzky). Presumably rats with elevated metabolic rates require more carbohydrate than normal animals.

The case of the parathyroidectomized animal serves as a good example of the development of specific aversions, as well as specific hungers, in the absence of endocrine secretions. The parathyroid gland, you will remember, governs calcium and phosphorus metabolism in the body, in that after the parathyroid glands are removed there is a deficiency in calcium and an excess of phosphorus. These changes are reflected in the food preferences of the animal (Richter). It shows great avidity for calcium, increasing its intake of the material by three or four times. On the other hand, a marked aversion for phosphorus develops. When parathyroid tissue is transplanted into such a rat and the hormone is restored, it quickly shifts its preferences back to normal proportions.

In much the same way, extirpation of the adrenal glands leads to a great increase in salt intake. As you will remember, the cortex of the adrenal controls to a considerable degree the amount of sodium excreted from the body. Indeed, its extirpation causes a salt deficiency in the body. In this way a specific hunger for salt can be developed, and rats in a condition of salt need ingest several times the normal amounts of salt (Richter and Eckert). In fact, such animals show a preference for salt even in concentrations so weak that they cannot drink enough to satisfy their physiological needs for salt. If adrenal cortical hormones are injected, the hunger for salt disappears. Contrary to what you might expect, however, intact rats injected with desoxycorticosterone acetate show a marked increase in salt intake (Rice and Richter). While this adrenal hormone may cause salt to be retained, excessive amounts of it in the body may also make salt unavailable for metabolism. That, at any rate, is one possible interpretation.

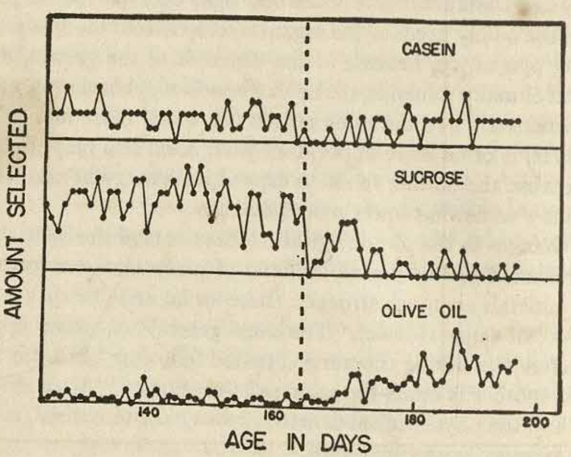

FIG. 138. Effect of removal of the pancreatic gland on the selection of elements of the diet by rats. The vertical dashed line indicates the day of operation. Note that with the diabetes created by pancreatectomy there is a decrease in hunger for sugar and an increased choice of fat (olive oil), which the animal can better dispose of. (*After C. P. Richter and E. C. H. Schmidt.*)

Vitamin Deficiencies. Specific hungers that develop in animals deprived of vitamins are particularly interesting. In the first place, such animals show specific hungers only when deprived of certain vitamins but not others. When deprived of vitamins A and D, for example, rats give no evidence of recognizing these elements in food, for they choose diets containing them no more than they do diets without them (Wilder). Neither does their preference change in pantothenic acid deficiency, although it is easy to demonstrate specific hungers for the rest of the B complex (Scott and Quint). A second point of interest is that animals suffering vitamin deficiency show changes in specific hungers for other foods, depending on how these are related to the metabolic action of the missing vitamin (Richter and Hawkes). For example, it is significant, in the light of the essential role of thiamin in carbohydrate metabolism, that thiamin-deficient rats cut down their intake of sugar and increase their fat intake. Similarly, they eat less protein in deficiency. In both these cases the rats go back to eating normal proportions when the vitamin is restored to the diet.

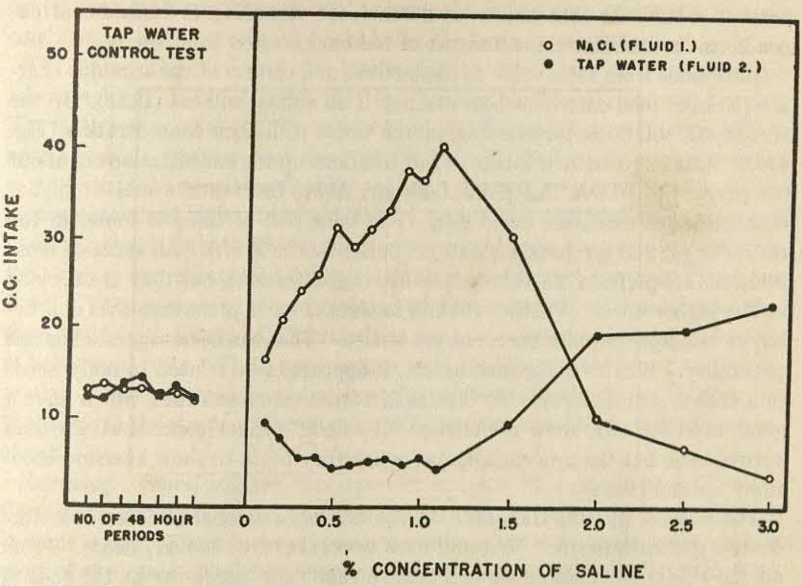

FIG. 139. Preference-aversion function of 10 rats to increasing concentrations of sodium chloride. Each point is based on 48 hr. of intake. For the first 7 days tap water was offered in two bottles. After that, salt was added to one bottle, and the concentration was increased every 48 hr. (*After J. K. Bare, 1947. See also J. K. Bare. The specific hunger for sodium chloride in normal and adrenalectomized white rats, p. 244. J. comp. physiol. Psychol.*, 1949, 42, 242–253.)

Stimulus Characteristics of Food. Perhaps we can understand why animals sometimes fail to select badly needed foods if we remember that animals must be able to discriminate foods if they are to select them. In this connection it is significant that rats, which do not show a preference for pantothenic acid, are able to select it accurately when it is flavored with anise, although they normally have no preference for anise (Scott and Verney). Conversely, thiamin preference can be temporarily broken down if the thiamin-containing food is first flavored with anise and then the flavor is shifted to thiamin-deficient food. For a time the animal continues to prefer the flavored food and fails to get thiamin, but after a while the preference shifts back to thiamin again. Again we see how learning food habits can obscure specific hunger. Even more important is the fact that ability to select foods according to body needs depends on the stimulus characteristics of the food.

Quite aside from their value as distinctive cues, certain of the stimulus characteristics of food determine how much of it an animal will eat (Bare). In the case of salt solutions, for example, intake varies with their concentration (Fig. 139). Rats increase their intake of salt solutions up to concentrations of about 0.9 per cent. Above this point they cut down their intake and at higher concentrations definitely avoid salt. The same sort of thing is found in the case of sugar and saccharine selection (Beebe-Center *et al.*). All three of these solutions are preferred to water at the low concentrations, but they are avoided at the higher ones. Whether the mechanism of such preference-aversion behavior is simply one of taste is not yet settled. That has been suggested as one possibility. Whatever the mechanism, it appears to be related to body needs in a rather complex way. To illustrate, adrenalectomized rats, which have a great need for salt, show preferences for salt at weaker concentrations than normal rats, but the concentration at which they begin to show aversion is entirely normal (Bare).

The Basis of Specific Hungers. As you can see, a number of different factors control specific hungers. First and most important are the body needs. From all the evidence available we can believe that body needs are at the root of food preferences and selective food intake. Second in importance is the detection or identification of the needed food. This aspect of the behavior depends upon the stimulus characteristics of the food. Its taste or smell most likely serve as cues, but other stimuli may sometimes serve too. Third is the experience of the animal—its learned preferences and aversions. As you have seen, food habits may facilitate or inhibit the selection of food in accordance with body needs.

All these factors may be at work in the selection of food under the influence of specific hungers. The big question, of course, is how they work. How do the body needs of the organism lead to fairly precise patterns of adaptive food-taking behavior? What are the mechanisms that regulate the animal's capacity to detect and select foods appropriate to its body needs? How does the animal adjust its intake to meet varying physiological requirements, when it needs anywhere from a few thousandths of a gram of one food to 10 grams of another?

Sensory Thresholds. One theory of specific hungers has been most popular. It is that body needs lower the animal's thresholds for tasting the substances needed (Richter). The change in taste threshold presumably lets the animal find and select more readily the food it needs. About this theory we can say that there never has been any direct demonstration of local changes in taste receptors as a result of specific body needs. It has been shown in the case of adrenalectomized rats that sectioning the taste nerves destroys the capacity to select salt, even though the body need is extreme (Richter). Furthermore, since adrenalectomized animals show a preference for salt solutions at concentrations far lower than normal animals do, it has been suggested that the condition of salt need actually does lower the taste thresholds.

Of course, the fact that the 'preference threshold' for salt is lowered in adrenalectomy does not mean that the 'sensory threshold' has been lowered. The failure of normal animals to prefer salt at the weak concentrations tells us nothing about whether they can taste it or not. In fact, it has been shown recently that the normal rat's ability to taste salt may be just as sensitive as the adrenalectomized rat's. In a very careful study, Bare and Pfaffmann measured taste thresholds in rats by recording nerve impulses in the taste nerves when the tongue was stimulated by salt solutions of different concentrations (see Bare). They compared the normal and adrenalectomized rats and found that they could both detect salt solutions as weak as adrenalectomized rats prefer in behavioral tests. These experiments indicate that the ability to taste is essential in salt selection, but that lowering of taste thresholds is probably not the factor in the strong preferences for salt that rats show when they are in need of salt.

Learning. Some suggest that specific hungers may be learned (Young). Certainly learning can help to explain the success or failure of food selections in some cases. There is no evidence, however, that it is necessary to explain most of the cases of specific hungers. More research is obviously needed before we can assign the proper roles to learning, taste sensitivity, or any other factors in specific hungers.

Whatever specific mechanisms are involved in specific hungers, they must ultimately work through the central nervous system. Unfortunately, we have very little information on the importance of the central nervous system in specific hungers. One preliminary experiment with a small number of rats has shown that the hypothalamic lesions that produce hyperphagia do not alter the proportions of foods eaten in self-selection tests (Brobeck *et al.*). Beyond this, however, we have no information about the central nervous system and specific hungers.

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CHAPTER XIX

INSTINCTIVE BEHAVIOR

Instinctive behavior is not easily defined. In the past many unfortunately have applied the term *instinct* rather loosely to any complex behavior that was not understood very well. Eventually the category of instincts became so broad that it was meaningless. At one point in history it was almost completely abandoned.

The trouble was that people, including many scientists, were regarding instincts as mysterious forces or inner urges which directed the behavior of the organism. Once it was decided that a particular kind of behavior was instinctive, it was considered explained and no further efforts were made to investigate its causes. In recent years, however, we have learned much from studies of the specific factors controlling instinctive behavior. Most of the confusion and mystery surrounding the earlier conceptions of instincts have disappeared. In fact, at the present time there is no real need for the term instinct, except as a conventional rubric for referring to certain kinds of complex motivated behavior.

It is not hard to understand why there was once so much confusion about instincts if we stop to consider how complex the factors are that control them. Like other kinds of motivated behavior that we have discussed, instincts are under the combined control of stimuli in the external world and subtle changes in the internal environment. As you will see, however, the internal and external factors controlling instinctive behavior are even more complex than those involved in simple bodily needs like hunger and thirst.

PERCEPTUAL FACTORS IN INSTINCTIVE BEHAVIOR

As Lashley has pointed out, one of our worst problems in analyzing instinctive behavior is to define the stimulus conditions that arouse any particular pattern of response. First of all, there are some cases where no specific sensory stimuli seem to be necessary to elicit the behavior. On the other hand, in many other kinds of instinctive behavior, a whole variety of different sensory cues are capable of calling out the behavior, or at least certain parts of it. Finally, the problem of the sensory control in instinctive behavior is complicated even more by the fact that certain conditions of the internal environment normally must prevail before any stimuli will be effective or before the behavior will appear at all.

Sensory Deficit. In many kinds of instinctive behavior we can discover no specific stimuli that are essential for the behavior pattern. The spider, for example, can spin an intricate web of a specific design over and over again, and the only condition it seems to need to start this behavior is to have no web. The same is true of nest building in birds. Certain birds build nests that are characteristic of their species whenever the appropriate building materials are available. The surprising thing is that even though the behavior pattern itself may be quite variable from time to time, the same kind of nest is always built. In this type of instinctive behavior there seems to be a sensory deficit which impels the animal to work until the deficit is corrected. To put it another way, the animal reacts to the *absence* of the stimulus situation provided by the nest or web and behaves somewhat randomly until a satisfactory stimulus situation is obtained.

Sensory Cues. In other kinds of instinctive behavior, specific stimulus objects in the environment are most important; *e.g.*, the female rat in heat arouses the male to sexual activity. Exactly what the male reacts to, however, is hard to say. We know that rats do not depend on visual, olfactory, or tactual cues alone, because eliminating any one of these does not interfere with the behavior (Stone). Sensory cues, therefore, may often be *alternatives* to one another in calling forth instinctive behavior. In other instances, sensory stimuli must be present in *combination* to elicit instinctive patterns. Gulls, for example, will retrieve eggs or any other oval objects of similar texture, but only if they can bring them to nests with which they are familiar (Borovski). Finally, it may be the *succession* of various stimuli that is important. In the migration of salmon, which we shall consider below, the path back to the spawning grounds depends first on chemical conditions in the water, later on the pressure of moving water, and finally on the temperature of the water.

Internal Environment. Certain conditions in the internal environment normally arouse instinctive behavior just as they do the patterns connected with bodily needs. Sometimes the internal conditions are periodic changes in the endocrine balance of the organism. In other cases they are caused by changes in the external environment such as temperature or amount of daily light. Finally, although the internal environment is normally important, there are times when it has little to do with instinctive patterns. Sensory stimuli and internal changes apparently act together to trip the central nervous mechanisms that are responsible for instinctive behavior, and some of the time sensory stimuli alone can excite the proper neural circuits.

MIGRATION

The migratory behavior of many animals, particularly that of birds and fishes, has long puzzled students of animal behavior. To the layman the explanation of this remarkable behavior has often been merely a matter of ascribing special instincts to the animals. The scientist, however, is interested in the specific factors that control the behavior. He asks three fundamental questions about migration. (1) What instigates it? (2) What factors control the course of travel? And (3) why do migratory animals go where they do? Some progress has been made in answering these questions, but owing to practical difficulties in experimenting with migration, there is still much to be learned.

The Migration of Fishes. In the case of migration of salmon we know something about each of these three questions. The facts of their migration are simple. Their place of birth and early growth is far up in the headwaters of streams. In their second year they migrate downstream to the ocean and there spend two or three years. After that they reenter the river, usually the one from which they came, and proceed up the river and its tributaries to its headwaters. There they spawn and die. Of course, not all salmon successfully complete these two phases of migration. Some may become lost, either going downstream or coming back upstream, and others may take an extra year in any phase. Much of the time, however, they do migrate successfully. The question is how they do it.

The first phase of migration is controlled by light. The salmon has some photosensitive receptors deep in its skin (Roule). In the young salmon these receptors are first covered by a layer of pigment, but gradually the pigment is lost. Then, of course, the photosensitive receptors are stimulated and the fish reacts negatively, *i.e.*, avoids light. Since the upper streams are shallow, this light-avoidance reaction eventually takes the salmon downstream to the deep ocean, where it gets away from a lot of light. Because the waters of the river emptying into the ocean are somewhat colder, contain somewhat more oxygen, and are less salty, the salmon tends to stay in the general region of the ocean into which the river runs.

Eventually the salmon matures sexually and its gonads put out more sex hormones. These raise its activity and probably its general metabolism, which in turn leads it to choose the colder and more oxygenated water at the mouth of the river. Once the salmon gets back into the river it has a strong tendency to swim against the current, a reaction known as a *rheotropism*. As the fish swims upstream and comes to each branch of the river, it chooses the one that is colder. This point has been established in a careful study of the temperature, size, and speed of flow of the streams chosen by salmon in their migration upstream (Ward). The salmon arrives eventually at one of the headwaters of the stream, usually the one that is coldest. There it lays its eggs and dies, thus closing one cycle and beginning another. Because of the factor of temperature in the route of migration upstream, it turns out that salmon tend to return to the same places in which they were born. Thus what may seem to be a mysterious instinct or a phenomenal memory for their places of birth is really a matter of reaction to particular stimuli in their environment.

The Migration of Birds. In birds, just as in salmon, there are a number of factors in the internal and external environments that control migration. One of the old and well-established facts is that the gonads change at the onset of migration. The change apparently is brought about indirectly through the effects of light on the pituitary gland (Rowan). In one experiment, two groups of snowbirds were kept in cages under identical conditions of temperature and feeding. For one group, the illumination each day was gradually shortened just as the day shortens in the fall. The other group had artificial days that gradually lengthened over a period of time, simulating the changes that occur in the spring. The gonads of the first group had hardly changed at all by the end of the experimental period. When they were released from their cages, they did not move away from the vicinity. The gonads of the second group, on the other hand, grew considerably, and many of them flew away when they were released. Since snowbirds fly north in the spring migration, we might suppose that the gonads increase their metabolism, which leads them to choose the colder temperatures. Whether this is so has not been definitely established, but light and hormonal changes are certainly associated with the onset of migration.

There are also other factors that may often be at work in the migration of birds. In some species migration occurs whether or not there are changes in light and even when the birds are castrated (see Beach). To explain such cases, some have argued that the pituitary may have an inherent rhythm. This rhythm, they think, affects not only the gonads but also the thyroid gland, and as a result general metabolism of the body and the nervous system are directly affected. Whether or not this notion is correct, one thing seems clear in all these studies. In one way or another, the pituitary gland is the most important single factor in the onset of migration.

In this connection it is interesting to note that the pituitary gland is important in the migration of salamanders to the water when they come to the end of the land phase of their life cycle. Immature salamanders in the early stages of the land phase migrate to water if pituitary tissue is transplanted into their abdominal cavities or if they are injected with prolactin, a pituitary hormone (Chadwick). Perhaps other factors might do the same thing, but the pituitary is important.

Unfortunately, we know less about how birds *find their way* in migration than we do about what makes them start migrating in the first place. It is difficult, of course, to follow birds and check up on their arrival at the breeding grounds or home area, and that partly explains our ignorance. To the extent that it has been possible to trace migration, however, we know that birds can follow a migration route very well, even without the benefit of previous experience. In one study, for example, a group of newly hatched crows were held in cages in Alberta, Canada, for a month after all the adults had gone south toward Oklahoma. After the young birds were released, over 50 per cent of them were recaptured in a direct line southeast of their birthplace along the route to Oklahoma followed by their parents (Rowan). Other studies report remarkable success of birds in finding their breeding places, but we have not been able yet to find out what cues they use to guide the course of flight. For some possible answers to this question we must turn to the closely related studies of homing.

Homing. Although homing and migration are not alike in many respects, in each case the problem that faces the birds is much the same. The experimenter, moreover, has an advantage in studying homing, for he can control the conditions of flight much more readily than in migration.

We know that birds will home from completely foreign regions, but we also believe that they must have experience with the terrain near the home area. In one study, for example, pigeons that were kept caged all their lives failed to return home from as little as 80 miles away (Platt and Dare). Since birds that had been allowed to fly around the home coop homed very well, it was concluded that pigeons learn to use particular landmarks in finding their way home and the only problem for them is to locate the landmarks.

There is no doubt that birds can use particular landmarks in their home territory, but there is still the question of how birds find their home territory when released from distant points. Or even more puzzling, how can migratory birds navigate to places they have never been? One theory suggests that birds possess special sense organs that are sensitive to the earth's magnetic fields and that these organs guide them in their flight to the home area or breeding grounds (Yeagley). So far, however, such organs have not been discovered, and it has been impossible to show directly that birds respond to magnetic fields in the absence of any other cues (Griffin). The more likely hypothesis is that birds make combined use of all their senses, although we can be rather sure that vision is the most important of the senses for this purpose (Griffin).

Some flying experience is necessary, of course, before birds can learn to use sensory cues. We know, in fact, that they can learn not only to follow specific landmarks but also to follow certain general cues afforded by rivers, the position of the sun, and the prevailing winds. Leading us to this conclusion are experiments in which birds have been followed during homing or migration either directly by airplane or by capturing them on the ground (Griffin and Hock). These studies show that birds scatter in every direction from the point of release and do a great deal of circling and exploring before they head for home. Many of them, furthermore, never get home when they are let out in strange territory. Analyzing the flights of birds that get lost shows that they can be misled by following the wrong river or getting caught in the wrong wind. That many birds do get home successfully is due to the fact that many of the geographical, meterological, and ecological cues that they follow very often do lead them to some familiar landmark in the home territory or, if they are migrating, to the general vicinity of an area suitable for breeding.

HIBERNATION

Like migration, hibernation is a seasonal type of instinctive behavior. It occurs in many mammals during the winter months. At that time the supplies of food are low, the temperature is low, and the animal is therefore called upon to conserve its bodily resources to the greatest possible degree. The hibernating animal usually finds a secluded place in which it will be protected from both the cold and other, preying animals. There it spends the winter months in a deep stupor resembling sleep. When the cold lets up and the chances of obtaining food are better, the hibernation ends.

Seasonal Changes. The causes of hibernation are to be found in the seasonal changes that take place in both the external and internal environments. Hibernating animals, like other mammals, are normally warm-blooded creatures who keep their body temperature at a high level compared to that of their environment. Unlike other mammals, however, hibernating animals fail to maintain body temperature in the cold weather. Part of the reason for this failure may be that such animals cannot find enough food in the winter to maintain the high metabolism necessary to keep up body temperature.

Another important reason, however, is that hibernating animals seem to suffer from seasonal changes in some of their heat-regulating mechanisms (Kayser). Even when kept at room temperature in the winter, their pituitary, thyroid, and adrenal glands regress a lot in contrast to those of other mammals (Woodward and Condrin). These seasonal changes in the endocrines must be important in hibernation, for simply exposing the animals to cold in the summertime when their glands are more active is not usually enough to induce hibernation. Furthermore, we cannot get hibernation in animals that do not normally hibernate, no matter how cold we make the environment. Indeed, the adrenals and thyroids of such animals get more active in the cold, when these glands are less active in hibernating animals.

Temperature Changes. All the evidence on hand indicates that changes in temperature and in glandular function together cause hibernation (see Kleitman). The normal body temperature of the hedgehog, for example, is maintained at about 34°C. up to the point where the environmental temperature falls to between 14.5 and 17°C. At these temperatures, the body temperature fluctuates between 15 and 30°C. and the hedgehog behaves as though half asleep. Then, below environmental temperatures of 14.5°C., the animal goes into hibernation, and its body temperature stays about 1° above the outside temperature. As we pointed out above, moreover, lack of food may contribute to the onset of hibernation at low temperatures. For example, when squirrels are starved and made less able, consequently, to keep up their body heat, they will go into hibernation more readily than otherwise.

Endocrine Changes. That seasonal changes in the endocrines are also important in the onset of hibernation is indicated by a number of experimental facts. For one thing, injection of adrenalin or of thyroid extract awakens a hibernating animal—even though briefly. On the other hand, insulin injections, which lower blood-sugar level and reverse some of the effects of adrenalin, may help to bring on hibernation. As you might expect, furthermore, hypophysectomy aids hibernation in some animals when the temperature is lowered. Contrary to what one would expect, however, hypophysectomized hamsters do not become stuporous at low temperatures as they normally do. They build nests and store food with great vigor as the temperature is lowered. But when the temperature gets to the point where they would ordinarily hibernate, these hamsters show a sharp increase in their heat production, which is nearly double that of normal hamsters kept at these temperatures (Kayser). Apparently, then, it is a positive seasonal change in the functioning of the hamster's pituitary gland, rather than a mere reduction or elimination of its activity, that is important in hibernation.

Physiological Changes. Most of the other physiological changes that occur during hibernation are very much what one would expect (see Kleitman). (1) The metabolic level is much below normal. (2) Blood sugar is reduced. (3) The acidity of the blood is considerably greater than in normal conditions, for the blood apparently can carry more carbon dioxide at lower temperatures. (4) The heart rate is, as one might expect, very low. (5) Finally, the irritability of the nervous system, which is dependent upon a normal internal environment, is greatly reduced. The stupor of hibernation is the result.

One final physiological change is of particular interest. There is a pronounced increase in lymphoid tissue of the body during hibernation. This tissue is quite toxic. When injected into an animal it can produce loss of appetite, fall in body temperature, and reduction in metabolic rate. Such an increase in lymphoid tissue, we know, can be due to a lack of vitamin D. On the basis of that clue, one investigator fed hedgehogs doses of this vitamin at a time when they normally would be hibernating (see Kleitman). The animals, as a result, did not hibernate, even though they were kept at temperatures well below those ordinarily invoking hibernation. Animals to whom the vitamin was not fed or in whom the feeding was discontinued did hibernate, however. This striking result, unfortunately, was not based on a very large number of animals, and the experiment should be repeated before it can be fully accepted.

HOARDING

Another kind of instinctive behavior that seems to depend on seasonal changes is hoarding. Many animals, especially rodents, store large amounts of food in the fall of the year when it is relatively plentiful. To account for this fact, some of the older naturalists assumed that rodents always carried food back to their nests and that the greater the amount of food available, the more they carried. We can strongly suspect, however, that the lowering of environmental temperature in the fall is also an important factor in hoarding. In fact, one of the incidental observations made in the study of hibernation showed that hamsters, which normally store large amounts of food, increase the amount of hoarding they do as it gets colder (Kayser).

Neither naturalistic studies nor incidental observations, however, can tell us anything very definite about the factors that are important in hoarding. Fortunately, the laboratory rat also hoards under certain conditions. All one has to do to observe hoarding in rats is to let them have a large number of food pellets outside their home cages. If the conditions are right, they will run out and carry back as much as a month's supply of food within a few hours. It is to the conditions that call out hoarding in this laboratory situation that we turn our attention.

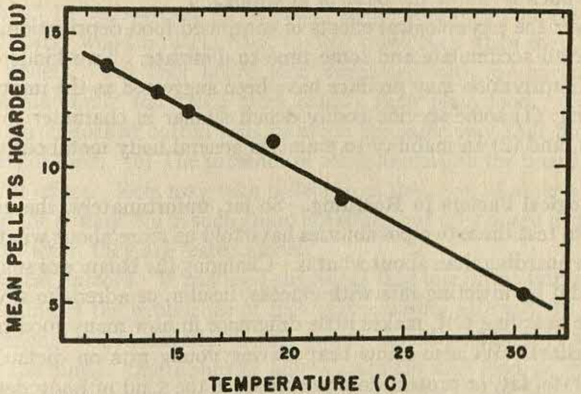

FIG. 140. Hoarding as a function of environmental temperature. Hoarding scores are in decilog units (dlu), computed by taking the logarithm of each score, multiplying by 10, and averaging for the group of rats. Each point represents 30 hoarding scores and 5 daily temperature readings. (*From R. A. McCleary and C. T. Morgan. Food-hoarding in rats as a function of environmental temperature, p.* 375. *J. comp. Psychol.*, 1946, **39**, 371–378. *By permission of the publishers.*)

Temperature. It turns out that temperature actually is an extremely important factor in the hoarding of the rat (McCleary and Morgan). At normal room temperatures, rats that have always had ample food carry back very few pellets from the storage bins. As the temperature gets lower and lower, however, they increase their hoarding activity more and more until they are carrying back more than ten times as many pellets as they can eat in a day (Fig. 140). Of course, we know that rats eat more and are more active when they are cold, and both these factors, as you will see, probably have something to do with hoarding.

Food Deprivation. One of the earliest studies of hoarding in the rat showed clearly that food deprivation was an important factor in the production of hoarding (Wolfe). Merely making rats hungry, however, is not enough to make them hoard. In fact, if rats are very hungry when they are given access to the food pellets in the storage bins, they will eat rather than hoard. The important thing seems to be some cumulative effect on the animals, produced by keeping them on restricted feeding for a week or more (Morgan *et al.*). Once these effects of deprivation have been built up, rats continue to hoard for some time after they have been satiated with all the food they can eat. Obviously, hunger as such is not at the basis of hoarding.

Whatever the physiological effects of continued food deprivation, they take some time to accumulate and some time to dissipate. Two kinds of changes that food deprivation may produce have been suggested as the important ones in hoarding: (1) some specific bodily deficit similar in character to a vitamin deficiency, and (2) an inability to maintain general body metabolism at a high level.

Physiological Factors in Hoarding. So far, unfortunately, the experiments designed to test these two possibilities have told us more about what is not important in hoarding than about what is. Changing the balance of sugar reserves in the body, by injecting rats with glucose, insulin, or adrenalin several hours before the hoarding test, makes little difference in how many food pellets they carry (Stellar). We also know that rearing young rats on diets deficient in carbohydrate, fat, or protein does not produce the kind of body deficit that is important in hoarding (Bindra). If there is a specific bodily deficit that induces hoarding, it is not the lack of any one of the major foodstuffs.

There is some support for the possibility that repeated deprivation produces an effect on metabolism that is important in hoarding. The effect of lowered environmental temperature on hoarding, for example, suggests that hoarding may occur when an animal is faced with increased demands for heat production or heat conservation. This interpretation implies that the thyroid gland may be important in hoarding as it is in both general bodily activity and nesting behavior (see below). Reducing an animal's capacity to maintain normal heat production by thyroidectomy or thiouracil treatment, however, has no effect on hoarding (Stellar). Neither does increasing heat production by thyroxine injection. Both these tests of the role of the thyroid were conducted at room temperature, however, and it may be that the animal's ability to control heat output is not so important under such conditions as it is under the influence of lowered temperatures. Much more research obviously is needed before we can say what physiological consequences of food deprivation are the important ones in hoarding.

Stimulus Factors. A large number of studies dealt with the environmental factors that influence hoarding. The following are some of the more important results that have come from these investigations (see Morgan). (1) Rats hoard more to a home cage with which they are familiar than to a strange one. Particularly important in this connection is the smell of the cage. (2) Hoarding is also greater when animals have been adapted to the hoarding alleys that lead to the storage bins. Once they are adapted, however, placing bright lights over the alleys and keeping the home cages dark easily doubles the amount of hoarding. (3) The amount of food rats have in their cages does not determine hoarding. One can either remove hoarded pellets from the cage or add many more pellets than an animal would ordinarily carry without affecting hoarding. (4) The object to be hoarded, on the other hand, is a very important factor. Rats do not carry wooden blocks back to their cages even when they are mixed with food pellets. Yet they hoard food sweetened with saccharine or food wrapped in aluminum foil much more readily than plain food. (5) Thirsty rats hoard water-soaked cotton rolls in much the same way that hungry rats hoard pellets of food. (6) The presence of other animals in the hoarding situation has little effect. Rats may take pellets from the cages of other animals as well as from the storage bin in such group hoarding, but they hoard neither more nor less than when they are tested alone.

Psychological Factors. It has been suggested that one of the important factors in hoarding is the experience of frustration during attempts to get food. Two experiments relate directly to this point. In one, adult rats were kept hungry all the time. One group of animals always had food in their cages which they could see and smell but could not reach. The other group was kept just as hungry, but every time they were given food they were allowed to eat it. In a subsequent hoarding test, the frustrated animals of the first group hoarded more food than the controls (McCord). In a similar study, rats were frustrated during infancy by keeping them on restricted feeding for two weeks right after weaning. When they were given an opportunity to hoard as adults, after five months of abundant food supplies, the frustrated animals hoarded many more pellets than their litter-mate controls (Hunt; Hunt *et al.*). In both these experiments, however, food deprivation was the crucial factor in calling out the hoarding, for the animals had a period of restricted feeding before the tests. Over and above the effects of deprivation, however, the kind of experiences animals have with food are important.

Neural Factors. While food deprivation may be one of the more important conditions for hoarding, a number of other factors are also important. For this reason one might expect that the central nervous system would be very important in hoarding. Unfortunately, we have very little information on this question. One experiment, recently completed, shows that removal of any part of the cortex of rats causes an increase in hoarding (Zubek). It is too early to be certain of the interpretation of this finding, but hoarding apparently is a relatively primitive kind of behavior that expresses itself better in the absence of the newer parts of the brain. Obviously, more research is needed before we can tie together the various facts of hoarding or state with any certainty what the nervous system does in it.

NEST BUILDING

Although nesting behavior goes along with mating and maternal behavior in many mammals and birds, it is a special type of instinctive behavior in its own right. For one thing, nest building may occur quite apart from mating or maternal behavior. Furthermore, male animals often build nests just as readily and just as actively as females.

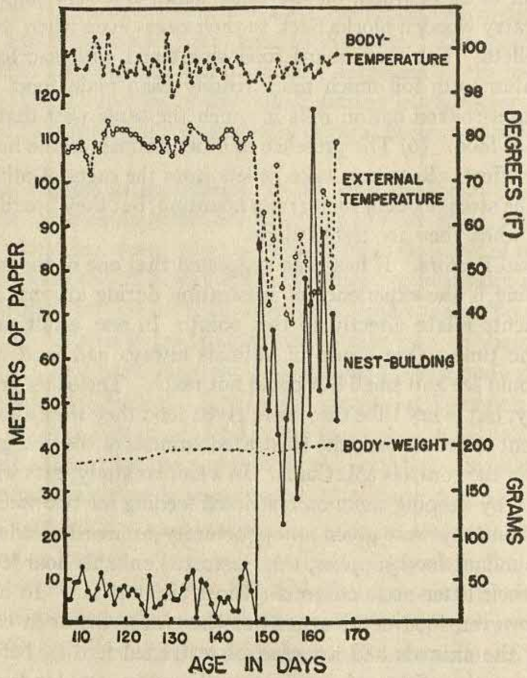

FIG. 141. The relation of external temperature to nest-building behavior in the rat. (*Based on work by E. Kinder. After C. P. Richter. Hypophyseal control of behavior, p. 265. Cold Spr. Harb. Sympos. quant. Biol.*, 1937, 5, 258–268.)

As in the case of other kinds of instinctive behavior, we are interested here in the specific factors that control nest-building behavior. For this purpose, of course, we need to have quantitative measures of the behavior, and fortunately, we have them. We can measure the nest-building behavior of rats, for example, by simply letting them have small strips of paper or a roll of paper that automatically turns a counter as it is unrolled.

Temperature. One of the first experiments with nest-building behavior dealt with environmental temperature (Kinder). The experiment showed that nest building, like hoarding, is inversely related to environmental temperature

(Fig. 141). At room temperatures or above, rats take very little paper into their cages and at most make very small and loosely constructed nests. At lower temperatures, however, their nest-building activity increases greatly, and they may fill their cages with several hundred feet of paper woven into tightly packed, well-constructed nests. Nesting behavior apparently serves as a heat-conserving activity which animals try whenever they lose much heat or when they badly need to produce heat.

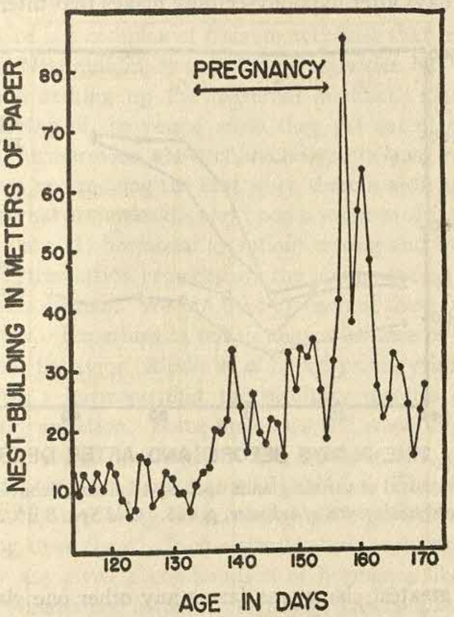

FIG. 142. Increase in nest building during pregnancy. (*After C. P. Richter. Hypophyseal control of behavior, p.* 265. *Cold Spr. Harb. Sympos. quant. Biol.*, 1937, 5, 258–268.)

Estrus and Pregnancy. The relationship of nesting behavior to estrus and pregnancy fits in very well with the notion that nesting is heat-conserving behavior. During estrus, when running activity and general metabolism are high, nest-building activity is at its lowest ebb (Kinder). During pregnancy, on the other hand, when activity and heat production are low, nesting reaches its highest level. Similarly, when a female becomes pregnant, estrual rhythms drop out, metabolism is low, and very shortly afterward nest building increases (Fig. 142). Toward the end of pregnancy, nest building reaches its highest level and remains high there until about 20 days after parturition. At this time the estrual rhythms begin again and the young rats are normally weaned.

Endocrine Factors. Experiments with endocrine glands, like those with estrus and pregnancy, give us support for the view that nest building is part of the temperature-regulating mechanisms (Richter). After removal of the hypophysis, for example, nest building increases nearly 200 per cent (Fig. 143). Extirpation of the adrenal glands results in a 24 per cent increase; of the gonads, a 50 per cent increase; and of the thyroid, about 100 per cent increase. As in the case of running activity, most of the effects of hypophysectomy are not direct effects but rather come through secondary atrophy of the other endocrine organs. At least, the fact that changes in nest-building activity do not occur for several days after hypophysectomy makes that interpretation reasonable. Since the greatest change, as far as any other one gland is concerned, follows thyroidectomy, changes in metabolic level appear to be the route by which hypophysectomy increases nest building.

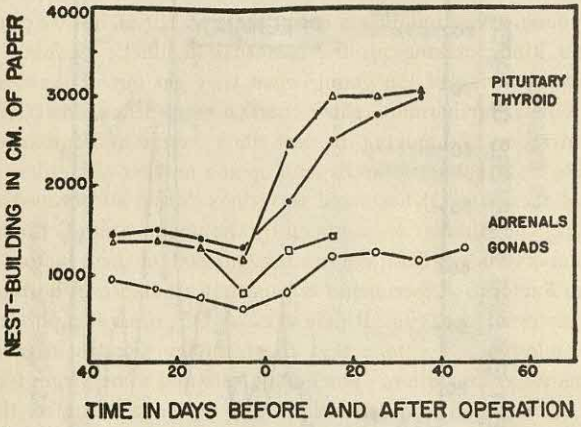

FIG. 143. Effect of removal of various glands upon nest-building behavior in the rat. (*After C. P. Richter. Hypophyseal control of behavior, p.* 265. *Cold Spr. Harb. Sympos. quant. Biol.,* 1937, 5, 258–268.)

Neural Factors. To establish the relationship between nest building and temperature regulation is not the same, of course, as explaining this instinctive behavior. We must ultimately understand nest building in terms of the influence of thermal changes on the nervous system. At present we know that there are definite centers in the nervous system for the regulation of body temperature. One pair is in the hypothalamus, and they are separate for cold and heat: the anterior hypothalamus reacts to heat (parasympathetic), and the posterior region responds to cold (sympathetic). Another center sensitive to temperature changes is in the ventral portions of the cerebral hemispheres. Since animals with lesions in the posterior hypothalamus cannot maintain body temperature, we would strongly suspect that damage to this area would produce vigorous nesting activity. Unfortunately, however, we have no studies of nest building in animals with lesions of any part of the hypothalamus or the ventral cortex.

Quite aside from the neural centers that are important in the regulation of temperature, we can expect the nervous system to play its part in carrying out nest-building behavior. We do, indeed, have some data on this point, but they have all been found in experiments with maternal behavior. We shall take them up, therefore, in the next section, which has to do with maternal behavior.

MATERNAL BEHAVIOR

Maternal behavior is a complex of discrete activities that center around the care of the young. Nest building is one of these activities, but we can recognize several other kinds making up the maternal 'instinct': cleaning the pups, nursing, and retrieving of the young when they get out of the nest. Many maternal animals, furthermore, show characteristic defense reactions such as attacks on intruders and moving the nest when there is a disturbance. As you will see, these maternal activities depend upon a number of factors. The most important of them are (1) hormonal secretions during and immediately after pregnancy, (2) the stimulation provided by the young, and (3) the integrative action of the nervous system. We can take up each of these factors in turn.

Endocrine Factors. Experiments tell us that a balance of hormones is important in maternal behavior (Riddle *et al.*). Of primary importance in this balance is *prolactin*, a hormone that the pituitary secretes in pregnancy to stimulate mammary secretion. Some male rats and some virgin females may show signs of maternal behavior without this hormone, but after they are injected with it they show much more maternal behavior. They react much more to young pups, readily retrieving them, and spend a good deal of time licking them and hovering over them. Such animals show even more maternal behavior when they are given a combination of hormones like that normally found in pregnant females just before parturition. This combination is gonadotropic hormones given somewhat before injection with prolactin.

These are not the only hormones that bring out maternal behavior. Others will do it too, although in lesser degree. Both progesterone and desoxycorticosterone are in this class, and for some reason yet unknown, so is the drug, *phenol*. Without effect, however, are many other hormones such as the growth hormone or the follicle-stimulating hormone (FSH).

According to Riddle, the substances that bring out maternal behavior are effective partly because they inhibit production of the sex hormones. Supporting this view is the fact that castration helps call out maternal behavior in both male and female animals, whereas estrogen or large amounts of FSH stop both lactation and normal maternal behavior. It is also interesting that hypophysectomy greatly increases maternal behavior in both male and female rats. This effect apparently is due to a decreased secretion of sex hormones following hypophysectomy. At least, the increase does not occur if gonadotropic hormones are given to maintain the secretion of sex hormones after hypophysectomy.

Altogether, these experiments tell us that prolactin is the most important single hormonal factor in maternal behavior. Perhaps its major effect, however, is to suppress the sex hormones. It probably does that at the end of pregnancy and during the nursing period, when maternal behavior hits its peak. Prolactin, however, must also be credited with some positive effects of its own, for it is more potent in bringing out maternal behavior than any other substance that has been tried.

Stimulus Factors. The stimuli that the young provide for the mother have a good deal to do with maternal behavior. The age and size of the pups is one factor. Mouse pups about five days old, for example, call forth maternal behavior more easily than do pups fifteen days old (Leblond). Another factor is the identity of the young pups. Some maternal animals can tell their own young and retrieve only them. Others accept as many strange young as they see, and some animals have been known to carry more than fifty pups back to their nest in a short period of time. The amount of familiarity that animals have with pups is another factor in maternal behavior (Leblond). Those that spend more time with young pups show more maternal reactions. Untreated virgin females and males, which at first show little interest in pups, retrieve them, lick them, and try to nurse them after they have been with them for some time. In fact Leblond, who did these experiments, was so successful at developing maternal behavior in animals without using hormones that he concluded that the appropriate stimuli can set off the nervous mechanism involved in maternal behavior independently of hormones.

Neural Factors. We are unable at the present time to say much about how hormones or stimulus factors affect the nervous mechanisms of maternal behavior. We do know something about the importance of the cortex in carrying out the behavior. Beach has done an extensive study of various maternal activities of the rat. He has shown that damage to more than 20 per cent of any part of the cortex seriously impairs nest building, retrieving, nursing, and protection of the young. Rats with fairly large lesions can somehow do all these things, but they do not do them well, and as a consequence, many of their offspring die in the first few days after birth. Operated animals, for example, build small, loosely constructed nests. Furthermore, they adapt poorly to disturbing conditions and do not move their young as readily as normal rats do when an electric fan or heater is put near the nest. They do not clean newborn pups or gather them into the nest as well as do normal controls. Finally, the retrieving activity of operated mothers is much slower than that of normal rats and tends to be less perfectly carried out.

Maternal behavior can also be impaired by giving rats series of daily cerebral electroshocks during the last half of pregnancy (Rosvold). Although these shocks do very little gross damage to the cortex, they can disrupt many of its functional capacities and may impair the function of other parts of the central nervous system (see Chap. XXV). There is some evidence, on the other hand, that the shocks cause an endocrine dysfunction, for autopsies of some of the experimental animals in this study showed them to have atypical pituitary glands. Unfortunately we know very little about the effects of electroshocks on either the endocrines or the nervous system. Although no direct damage to the fetuses in utero could be found, it is even possible that some of the effects observed in this study were caused by the convulsions that follow the electroshocks.

Much more work is needed on the neural basis of maternal behavior. While the cortex is important primarily in the organization of the behavior pattern, it is likely that subcortical centers are the crucial ones in the arousal of the maternal instinct. We cannot say what these subcortical centers may be, but in the next chapter you will see how cortical and subcortical centers can work together in some other instinctive patterns of behavior.

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CHAPTER XX

MATING BEHAVIOR

We are devoting this whole chapter to mating behavior. Since it is only one of many kinds of motivated behavior, that may seem a bit out of proportion. There are, however, two good reasons for doing it. (1) Because of many diligent and ingenious studies by research workers, we know more about mating behavior than we do about any other kind of motivated behavior. (2) It turns out that mating behavior is an excellent example from which to draw general conclusions for all kinds of motivated behavior. Both these points will become clear as we go through the chapter.

Phyletic Comparisons. The facts about mating behavior have been found with many different animals in the vertebrate series from fishes to man. As you will see, mating behavior in the series is under the influence both of hormones and of the nervous system. In the lower vertebrates, moreover, mating patterns are constant enough to be considered "instinctive," and it is here that they are largely under hormonal control. In higher animals, mating patterns are more variable—particularly are they more subject to environment and learning—and the nervous system is relatively more important. As we go into the material of this chapter, it is therefore well to keep in mind that both hormones and nervous factors are always important in mating behavior but that hormones decrease and other factors increase as we go up the phyletic scale.

THE CHARACTER OF MATING BEHAVIOR

The patterns of mating behavior differ a great deal in different species of animals as well as in the two sexes. The basic pattern seen in most mammals and birds, as well as in many other lower vertebrates, has three main parts: (1) orientation of the two partners, which may involve elaborate courtship behavior; (2) postural adjustments involving elevation and exposure of the genitals in the female and mounting in the male; and (3) the occurrence of the genital reflexes until ejaculation of the male occurs. For our purposes, it will be sufficient to note briefly the behavior that appears in those warm-blooded animals which have been most commonly used as subjects in the study of the physiological basis of mating behavior.

Birds. Sexual (mating) behavior in birds may be divided into two types, primary (copulatory) and secondary (courtship) behavior. Courtship precedes and leads up to copulatory behavior. It consists of several rather distinct activities, among them billing and cooing (Carpenter). In billing behavior, the bills of the male and female are interlocked in such a way that the lower beak of the female is usually below that of the male, the upper half being in the mouth cavity of the male. With their bills interlocked, the birds move their heads up and down with a vigor and quickness that suggest excitement. Interspersed with this billing may be vocalization, charging, and strutting—all characteristic of sexual behavior. Charging and strutting have much in common, but charging is more characteristic of some animals (*e.g.*, pigeons) and strutting of others (*e.g.*, turkey and peacock). Such secondary behavior prefaces copulatory behavior and perhaps serves as a stimulus to it.

Courtship merges into copulatory behavior when the female assumes a submissive and receptive posture. This consists of a slight spreading of the wings, extension of the tail, and flexing of the legs, and is the posture that is conducive to copulation. The behavior of the male becomes dominant. He mounts the female and makes a balanced adjustment with his feet and wings, in some cases by grasping the feathers of the female's neck with his beak. Then copulation occurs and is followed by a period of inactivity, after which the sequence of mating activities may be reenacted. There are, of course, several variations in patterns of sexual behavior in the same animals and in different animals, but the highly organized character of the mating patterns is a remarkable fact worthy of special note (Carpenter).

Mammals. The mammalian animals whose mating activities have been most extensively studied are the cat, rabbit, guinea pig, and rat. The male sexual behavior of all these animals is quite similar. It consists in mounting, clasping the neck of the female in the mouth, and making pelvic thrusts (the basic copulatory movements). Patterns of mating behavior of the females of these animals are also highly organized in relatively stereotyped sequences—but they differ markedly in different species, as is indicated by the following descriptions (Bard). Receptive behavior of the female rat consists simply of tense crouching for brief periods, interrupted by quick darts about the cage and a great amount of running activity. When mounted, the female rat assumes the posture that allows the male to achieve intromission and copulate successfully. It consists of an elevation of the rump, together with a tense receptive posture. In the rabbit it includes also an adjustment of the tail. The guinea pig, along with this reflex pattern, frequently emits a characteristic vocalization.

Whereas the mating pattern of the female rodent is rather simple, receptive behavior of the cat is much more highly organized and conspicuous. It begins with courtship, which leads to copulation, which in turn is followed by an afterreaction (Bard).

> The courtship behavior includes playful rolling, excessive rubbing, a curious slow vocalization (the estrual call) and crouching and treading. The estrual crouch is a most specific posture. Resting on chest and forearms with pelvis raised somewhat

> and with tail elevated and turned to one side, the animal tends to execute treading movements of the hind legs. It is in this posture that the male is accepted. Many estrual cats crouch and tread quite spontaneously in the absence of any specific external stimulus. Others do not show this behavior unless they are in the presence of a male or receive some stimulation of the external genital region. . . . In most animals [the after-reaction] consists of more or less frantic rubbing, squirming, licking and rolling.[1]

Infrahuman primates exhibit fundamentally the same pattern of behavior in mating as the lower animals. In monkeys and chimpanzees, the female bends forward at the hips, presenting the genitalia, and the male grips her hind legs with his feet and clasps her hips. Occasionally chimpanzees will copulate in a face-to-face position. In this case the male keeps his feet flat on the ground and holds the female with his arms while she embraces him with her hind legs.

Bisexual Behavior. One important point to keep in mind is that the masculine and feminine mating patterns described above do not belong exclusively to males and females respectively. Both male and female animals are capable of both masculine and feminine patterns and often show them. For example, male rats will display feminine receptive behavior when agressive males attempt to mount them. Similarly females, especially when highly receptive, may often show mounting behavior characteristic of males. As you will see below, the behavior pattern of the opposite sex is readily brought out under experimental conditions where hormones of the opposite sex are administered (page 430). But the occurrence of bisexual behavior is independent of special hormonal conditions and is seen in all species of animals. Extensive studies of free-ranging monkeys, for example, show that males living in isolation will frequently alternate in playing the masculine and feminine roles (Carpenter). Such observations demonstrate that both males and females possess the neuromuscular mechanisms required in both patterns of mating behavior. Only the appropriate hormonal or external stimulation is necessary to make one or the other pattern prepotent.

GONADAL CYCLES AND MATING BEHAVIOR

From countless studies of mating behavior in different animals, we can say that mating behavior runs in cycles, *i.e.*, it has its ebbs and flows, its rises and falls. There are three main types of cycle that we can see: life cycles, seasonal cycles, and estrous cycles. All these cycles depend in one way or another on hormones. In some cases hormones are stimulated or depressed by other factors, but they usually are responsible for the cycles that we see. In this section we shall consider just how hormones, behavior, and other factors are interrelated in the cycles of mating behavior.

[1] Bard, p. 554.

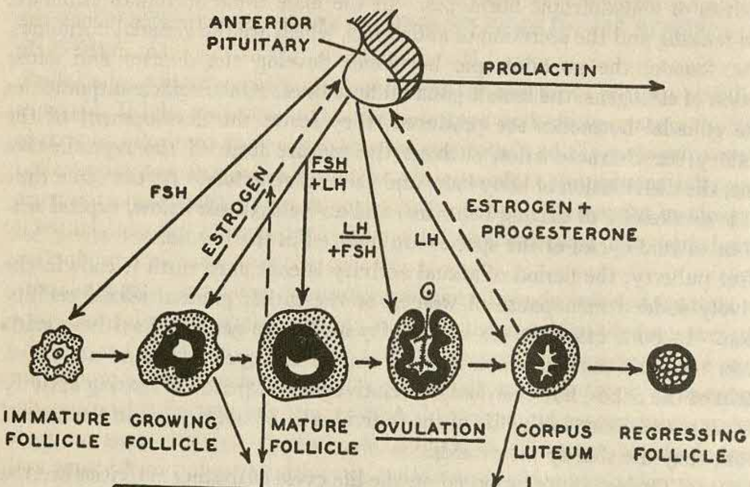
The Life Cycle. In every normal individual there is a single long period of mating activity, beginning with the maturation of the gonads at puberty. In some way as yet unknown, the anterior pituitary gland is stimulated to activity at this time in the life cycle and it begins to elaborate and secrete large quantities of gonadotropic hormones. In the male these hormones stimulate sperm making and the secretion of androgens, which are the gonadal hormones. In the female, the gonadotropic hormones develop the ovaries and cause secretion of estrogens, the female gonadal hormones. Once sufficient quantities of the gonadal hormones are produced, they foster the development of the secondary sex characteristics, such as the mature form of the reproductive organs, the distribution of body hair, and skeletal structure. At the same time there is awakening of mating behavior, and as we shall see below, typical seasonal or estrual cycles of the species are induced in the female.

After puberty, the period of sexual activity is continued until it ends in the relatively sudden menopause of women or the rather gradual sexual senility of men. In both cases the sexual activity and drive get lower as the gonads regress. Infrahuman mammals show a similar life cycle of sexual activities. Certain of the fishes, however, have a relatively short period of mating activity that occurs only once in the life of the individual. Sometimes, as in the case of salmon, they die shortly afterwards.

Seasonal Cycles. Superimposed on the life cycle of mating activities are the seasonal cycles of many animals. The seasonal rise and wane of such activity goes along with the growth and decline of the gonads, but the number and length of seasonal cycles varies in different animals. In the female dog, for example, there are two seasons of heat, one in the spring and another in the fall. Each lasts about 2 weeks. For the most part seasonal cycles appear only in females, but in some species (marten and deer) they appear in the male as well.

Studies of the cells of the pituitary gland, as well as its secretions, show that the seasonal cycles of the gonads go along with changes in the activity of the pituitary (see Moore). In animals that can breed at any time of year, the pituitary keeps up its activity all the year round; but in seasonal breeders it becomes active only near the breeding season. One of the factors that seems to be important in bringing the pituitary into action is the amount of light in the environment. In fact, all the hormonal and behavioral signs characteristic of the breeding season can be brought about out of season by artificially lengthening or shortening the amount of light every 24 hr. (Dawson). Light is not the only factor in the control of seasonal breeding, however. Seasonal cycles will occur in the female ferret, for instance, even after the optic nerves are severed (Bissonnette). On the basis of this kind of evidence, it has been suggested that the anterior pituitary has an inherent rhythm which can go on by itself but can be influenced by light cycles.

Estrous Cycles. Some animals are sexually active throughout the year. In most males, for example, mating can occur at any time, for they do not have variations in gonadal hormones after puberty. In females, however, there are short-run cycles in which sexual receptivity waxes and wanes with ups and downs in the activity of the ovaries. In infraprimate mammals these short cycles are called *estrous cycles*, and the high points of gonadal and sexual activity are called *estrus* or *heat*. From a physiological and behavioral point of view, estrous cycles correspond very closely to the menstrual cycles of primates. Both estrous cycles and menstrual cycles begin and end in a low point of sexual activity and ovarian development. At the midpoint of each cycle, about the time ovulation occurs, receptivity reaches a peak.



	ESTROGEN	ESTROGEN + PROGESTERONE			
UTERUS	EPITHELIAL CHANGES	UTERUS PREPARED FOR IMPLANTATION			RESORPTION OF EPITHELIUM OR MENSES
OVUM	IN FOLLICLE	IN TUBE	IN UTERUS	IMPLANTATION PERIOD IF FERTILIZED	
INFRA-PRIMATE RECEPTIVITY	NONE	"HEAT"	NONE		
INFRA-HUMAN PRIMATE RECEPTIVITY	MINIMAL	MAXIMAL	MINIMAL		

FIG. 144. Scheme of events taking place in the ovary and uterus during the estrous cycle, showing corresponding changes in the sexual receptivity of infraprimate and infrahuman primate animals.

The physiological events occuring during these cycles have been worked out in considerable detail. Some of the major ones will be of interest to us (Fig. 144). (1) Under the influence of the *follicle-stimulating hormone* (FSH) of the anterior pituitary gland, the follicles of the ovaries begin to develop. (2) As the immature follicle grows it secretes *estrogen*, and this, in turn, helps the anterior pituitary body to produce a second hormone, the *luteinizing hormone* (LH). (3) The combined influence of FSH and LH helps the follicle develop, and thus more estrogen is secreted. (4) Next, large amounts of estrogen change the epithelium of the uterus and vagina and at the same time influence the pituitary gland to secrete more LH and less FSH. (5) At this point in the cycle the follicle ruptures and releases the ovum. (6) After ovulation, the follicle begins a new stage of development and, under the influence of LH, becomes the *corpus luteum*. (7) As the corpus luteum develops it continues to secrete estrogen and, in addition, elaborates a new hormone, *progesterone*, often called the *hormone of pregnancy*. (8) Together, estrogen and progesterone cause more epithelial changes in the uterus until it is ready for the ovum to be implanted if fertilization takes place. (9) Progesterone also serves to stimulate production of the lactogenic hormone of the anterior pituitary, *prolactin*. (10) Prolactin, finally, is important in the development of the mammary glands for milk production, should pregnancy occur.

If pregnancy does not occur, the corpus luteum regresses and the production of estrogen and progesterone drops. As a result, the uterine epithelium developed by these hormones is resorbed or, in animals that menstruate, is sloughed off and eliminated. In addition, the withdrawal of progesterone and estrogen permits the pituitary to secrete sufficient quantities of FSH to promote follicle development and start another cycle.

If pregnancy does occur, the ovum is implanted in the uterus, and a placenta develops from the uterine epithelium and the developing blastocyst (immature embryo). When the placenta forms it secretes gonadotropic hormones similar to those of the pituitary gland, called *anterior-pituitary-like hormones* (APLH). These gonadotropic secretions serve to maintain the corpus luteum for a longer period than usual—about a month in humans. After the corpus luteum disappears, the placenta takes over the major endocrine functions and secretes the large amounts of progesterone and estrogen that are characteristic of pregnancy.

Sexual Behavior and Estrus. Closely correlated with the physiological changes of the estrous cycle are the variations in sexual receptivity seen in female animals (Fig. 144). The female rat, for example, has a 4- to 5-day estrous cycle and is receptive only during about six hours of this period. Usually heat occurs at night and can be identified by the appearance of cornified epithelial cells in the vaginal mucosa. When heat begins there is an increase in general activity of the animal. The rat also hops and darts about its cage fitfully, and it responds to pressure stimulation of the lower back with an arching of the back called *lordosis*. During the rest of the cycle the female rat is relatively inactive and shows no signs of sexual receptivity. In fact, the anestrous female will fight off any attempts on the part of the male to mount. Here is a clear-cut case of the peak of sexual activity in an animal corresponding to the peak of estrogen production by the ripened ovary.

Essentially the same behavioral changes are seen in the menstrual cycle of infrahuman primates. Monkeys and chimpanzees show heightened sexual activity at about the time of ovulation (Ball and Hartman; Yerkes and Elder). During this period the genitalia are characterized by reddening and swelling. The female in heat goes toward, and in general is sociable with, the male, whereas during anestrus the usual behavior is avoidance. In fact, the female in heat may actively try to attract the attention of the male and assume the specific receptive posture, thus 'presenting' herself. In the case of the chimpanzee at least, the female in heat becomes socially dominant even in nonsexual matters such as food taking, whereas in anestrus the male is dominant (Yerkes).

Despite this correspondence of sexual behavior with the high points of estrogen production during heat, female monkeys and chimpanzees may show some signs of sexual activity during anestrus. In humans, departure from physiological cycles is even more marked. Sexual activity will occur at any time in the menstrual cycle. In fact, one study shows that sexual desire in women is highest just before and just after menses rather than in the middle of the cycle (Davis). There is no apparent hormonal basis for this discrepancy between man and other primates. As you will see from other evidence, nonendocrine factors play an important role in human sexual behavior and may well obscure the relationship between the menstrual cycle and sexual activity.

Pregnancy and Estrus. In most infrahuman animals, sexual drive is notably lacking in the female during pregnancy. In rats, for example, there are no further estrual periods of heat once pregnancy is started. Throughout the period of gestation, the female will not be receptive to the male. But a few hours after birth of the young a period of estrus ensues, and impregnation may take place at this time (postparturitional heat). Immediately following this period, however, the mother goes into anestrus and does not display heat again until the end of the nursing period, about 21 days later. In spite of the lack of sexual drive and estrous cycles throughout these periods, there is a suggestion that ovarian cycles continue in pregnancy. In nearly all animals it is the common rule that the term of pregnancy is some multiple of the estrous cycle. Parturition seems to be associated, in fact, with the culmination of a cycle, for ovulation and postparturitional heat follow it closely. The hormonal causes of parturition, however, are obscure.

Photic Stimulation and Estrus. We have already mentioned that changes in the number of hours of light in a day are important in controlling seasonal cycles of sexual maturation and behavior. Light also affects estrous cycles. Estrus normally comes early in the dark part of a 24-hr. period and is accompanied by a characteristic burst of running activity. If the light-dark cycle is reversed, estrus and the burst of activity will come during the new dark period.

By keeping animals in constant light, moreover, the period of sexual receptivity can be prolonged although running activity cannot (Browman; Hemmingsen and Krarup). On the other hand, rats kept in constant darkness reduce their activity and show prolonged periods of anestrus, coming into heat far less frequently than normally treated rats (Browman). These facts suggest that there may be some cumulative effect of light on the organism which helps to induce estrus and to prolong it once it is started.

Many of the details of the mechanism that underlies the effects of light on sexual behavior in estrual and seasonal cycles have been worked out. Apparently light can affect the anterior pituitary through the optic-hypothalamic tracts and cause an increase in the production of gonadotropic hormones. We have direct evidence, in the case of the rat, that light will produce cellular and chemical changes in the pituitary that indicate pronounced gonadotropic activity (Fiske). Moreover, in some species (birds) we know that such pituitary stimulation results in maturation of the gonads (Rowan). Another related fact is that neither blinded nor hypophysectomized animals show the effects of artificial illumination on sexual behavior (Bissonnette). Extirpation of various visual centers of the brain, furthermore, shows that only the visual pathways to the subthalamus, hypothalamus, and pituitary need to be intact for light to play its role (Clark *et al.*). It must not be assumed, however, that the influence of light is crucial to estrous cycles, for they do occur in the total absence of light. There probably are inherent pituitary and ovarian rhythms which can be, but are not necessarily, controlled by light.

EFFECTS OF CASTRATION UPON SEXUAL BEHAVIOR

All that we have said so far points to the hormones as the mainsprings of sexual behavior. That is partly true, especially in females and lower animals, and not quite so true in males and in higher mammals. Let us look into the matter in some detail, however, and consider exactly what happens to sexual behavior when we step in and remove the glands that make the hormones.

Ovariectomy. It is well established that monkeys and lower mammals become sexually unreceptive after complete removal of the ovaries (Ball). The effect on sexual activity is the same whether animals are castrated before or after puberty. But if castration is done during estrus, sexual behavior may persist for a short time, owing to the presence of large amounts of estrogens. Very shortly thereafter, however, sexual receptivity disappears permanently. If activity records are used as an index of sexual drive, they show that the gonadectomy has permanently abolished sex drive, for the usual cycles of activity (4 to 5 days in the rat) are completely lacking.

In women, however, the effects of ovariectomy are not nearly so definite. Indeed, there are numerous observations that sexual desire undergoes no diminution following double ovariectomy (Frank). Yet comparatively good studies claim a gradual reduction in sexual desire and the capacity to carry out reproductive behavior properly (Clauberg and Schultze). In any event, it seems quite certain that ovariectomy does not promptly and permanently abolish sexual desire in all women. Here again we are confronted with a discrepancy between man and the lower animals. Apparently human sexual behavior is less crucially dependent upon the sex hormones than is the mating behavior of lower animals.

Male Castration. The effects of gonadectomy on male animals differ considerably from the effects of ovariectomy on females. It is generally true that a male castrated before puberty never develops normal mating behavior. If castration is performed after puberty, however, copulation occurs normally for a short period and then diminishes slowly. In rats, for example, 1 month after castration, 33 per cent of one group of castrates had ceased to copulate; after 2 months, 45 per cent would no longer copulate; and in the subsequent 4 months, more and more animals lost their sexual drive (Stone). First to be lost was the capacity to ejaculate, and only later did the copulatory pattern drop out. Opportunity to practice copulation had no apparent effect on the length of time that sexual behavior would survive castration, for animals allowed to copulate behaved the same as those that were segregated.

Studies of higher animals show that some important changes have taken place in the course of evolution in the role of the sex hormones in the mating behavior of the male. While some dogs, castrated after sexual experience, show impairment of mating, others will copulate for as long as two years after operation (Beach). Supporting this finding is the fact that castration may have only slight effects on the sexual behavior of the male chimpanzee. In fact, it has been reported that a prepuberally castrated male chimpanzee was capable of vigorous sexual activity in adulthood (Clark). Finally, although the data on man are not always in agreement, it seems to be the rule that sexual behavior will survive castration in adulthood and may even appear after castration before puberty (see Beach). In the sexual behavior of males, then, the sex hormones have become less and less important in the course of evolution.

Hypophysectomy. As you might expect, extirpation of the pituitary gland has an adverse effect on sexual behavior. The surprising thing about hypophysectomy, however, is that it has just as much effect on males as on females (Wiesner and Sheard). In both cases sexual behavior drops out rather promptly, and this effect seems to be permanent. It is not necessary, of course, to assume that the pituitary secretes a hormone that is crucial for male sexual behavior, for we know that it governs the activity of several other glands. It is entirely possible that the adrenal cortex, for example, secretes sufficient quantities of androgens to maintain sexual activity temporarily after castration. After hypophysectomy, regression of the adrenals, as well as of the testes, would be expected to reduce the supplies of androgens. So far no direct attack has been made upon this problem, but it would be interesting to see whether the effects of castration plus adrenalectomy are more serious than the effects of castration alone.

In females, hypophysectomy and ovariectomy have just about the same effects. Following hypophysectomy, sexual receptivity promptly disappears and the ovaries and secondary sex apparatus rapidly regress. If, on the other hand, the pituitary is not removed but its stalk is merely sectioned, female estrous cycles persist, but they are no longer of normal length or regularity. In rats on whom this operation was done, for example, Richter finds peaks of running activity occurring every 13 to 18 days rather than the usual 4 to 5 days. For this effect Richter suggests an explanation. The denervated pituitary, he believes, fails to respond properly to the cycles of ovarian secretion. As a result it fails to put out its normal amount of gonadotropic hormone, and the ovary in turn does not always swing the full extent in its cycle. The end result is that the period of estrus sometimes is skipped, and when it does appear it is some multiple of the normal cycle.

HORMONE ADMINISTRATION AND SEXUAL BEHAVIOR

As you can see, experiments with castration shed some light on the problem of hormones and sexual behavior. A natural partner of the method of castration is the method of replacement therapy, in which hormones in one form or another are used to treat animals (or people) suffering from various sorts of glandular deficiencies. In the last decade or two this method has become particularly useful because the biochemists have made so much progress in preparing the different hormones we need. We therefore now have a good deal to say about the effects of administering hormones under different conditions.

Reactivation of Castrates. As one might expect, it is possible to inject a gonadal hormone and offset the effects of removing the gonads. This will work in either male or female animals. In castrated male guinea pigs, for example, sexual behavior returns after treatment with testosterone (Seward). The effects occur in the rat and in all infrahuman primates, even those that have been castrated before puberty. In the male rat, it is interesting that treatment with gonadal hormones first restores the copulatory pattern and sometime later the ability to ejaculate—just the reverse of the order of loss after castration (Stone).

Unfortunately, our statements about man cannot be so definite (see Beach). In some cases injecting hormones in castrates seems to restore sexual potency and in others it does not. Of course, this is not surprising if we remember that castration in the first place sometimes seems to destroy sexual potency and sometimes not. So it looks as though psychological and other factors are important enough in man to obscure the effects of castration and replacement therapy.

Estrogen. The effects of replacement therapy with ovariectomized females are much the same as those seen in the male. In castrated female rats, the injection of estrogen brings about estrus and sexual receptivity (Ball). The estrous cycle, however, is not entirely normal, for sexual receptivity does not wax and wane periodically nor does bodily activity come back to its usual peak in estrus. On the other hand, castrated female monkeys given estrogen show definite signs of sexual periodicity (Ball). There is, furthermore, a definite relation between the amount of hormone injected and the degree of sexual responsiveness induced.

The results with ovariectomized women are no clearer than those obtained with castrated men (see Beach). Many positive effects of hormone treatment are reported, but there have also been many failures. Unfortunately, one cannot tell from the literature whether suggestion and other 'psychic' factors have been ruled out.

Combination of Hormones. Of particular interest is some research by Young and his collaborators in which estrogen and progesterone have been used together. In the guinea pig, it turns out, estrogen and progesterone given in sequence restore sexual behavior, as well as physiological signs of estrus, more effectively than estrogen alone (Boling *et al.*). Species of animals differ, however, in their response to the combination. Most rodents react like the guinea pig. But receptivity in rabbits as well as in monkeys is actually inhibited by giving them progesterone; in castrated female monkeys it partly counteracts effects of estrogen in restoring sexual behavior (Ball). Clinical reports say that progesterone also lowers the sexual desire of women (see Beach). All this, of course, fits in with the absence of sexual activity during pregnancy, when production of progesterone is high.

Reactivation of animals whose sexual drive has been lost as a result of hypophysectomy is also possible. Injection of gonadotropic hormones will cause the gonads to mature again and will restore mating behavior. Gonadal hormones will do the same thing, so we know that the pituitary and its secretions are not crucial for mating behavior as long as there are adequate amounts of sex hormones.

Induced Mating in Normal Animals. Since there are many times in the life of normal animals when they are not sexually active, it would be interesting to know whether sex hormones can restore sexual activity at these times. Three kinds of studies bear directly on this question: (1) induction of mating behavior in immature animals, (2) stimulation of animals to breed out of season, and (3) reactivation of animals that have lost sexual powers in senility. All these studies are approaches to the question of whether animals that are inactive presumably because of lack of gonadal hormones are otherwise equipped to carry out mating behavior. As you will see, this possibility turns out to be true in some cases but appears not to be in others.

Premature Development. Giving either gonadotropins or gonadal hormones to immature animals, either male or female, makes them sexually active at an early age (see Beach). Female rats given anterior pituitary extracts show signs of estrus at twenty-two days of age, although they normally do not show them until about fifty days. Just about the same thing happens when they are given estrogen. Similarly, male rats given androgen on the fourteenth day show sexual mounting as early as the sixteenth day. Similar reports have been made for mice and dogs. Taken together they make us believe that the neuromuscular mechanisms of sexual behavior are matured at a very early age and that they simply wait to show themselves on the development of the gonads and their hormones.

Activity out of Season. In many species that breed seasonally, sexual behavior can be induced off season in several ways (see Beach). One way, as we saw before, is by changing the light in the environment. Another is by injecting gonadotropic or gonadal hormones. Similarly, in polyestrual animals like the rat, these same methods can be used to bring on or prolong periods of heat. Thus we see again that hormones can arouse the neuromuscular mechanisms quite apart from naturally occurring cycles.

Decline with Age. Sexual potency, of course, also declines in man and animals as they get into old age. In lower animals, hormones sometimes succeed in bringing back sexual potency. In one study, for example, rats that were twenty-eight months old and had virtually ceased to copulate were reactivated by injections of testosterone (Minnick *et al.*). Other studies of lower animals have made similar claims. In man, however, the effects of hormones are not clear, and they frequently fail to restore sexual potency. That should not be too surprising in view of the fact that human beings can lose sexual potency even when they have adequate hormones. We know too that psychological factors are more important in human sexual behavior than in lower animals.

Specificity of Sex Hormones. So far we have dealt only with the effects of male hormones on male animals and of female hormones on female animals. There are, of course, other possibilities. In fact, they raise the interesting question of what different kinds of hormones have to do with different patterns of behavior in the two sexes. Fortunately, there are a great many experiments on this question, and Beach has summarized them for us in Table 6. There you will see that

1. In both male and female castrates, androgen brings out masculine sexual behavior and estrogen feminine behavior. The sex of the animal, however, is of some importance, for it takes less male hormone to elicit masculine behavior in males than in females, and vice versa.

2. Androgen can bring out feminine behavior and estrogen masculine behavior in animals of both sexes. In such cases, however, it takes extremely high doses of hormones to produce rather slight effects in sexual behavior.

3. Under some circumstances, when an animal receives hormones of the opposite sex, its sexual behavior may be inhibited. When androgen is given to normal females, for example, it often inhibits feminine responses and facilitates

masculine responses. The converse happens with estrogen given to males. Results such as these may simply mean that one set of responses is dominant over the other and not necessarily that there is any true inhibition by the hormone.

4. Male hormones given to males and female hormones given to females may inhibit the development of normal mating behavior if they are administered in large doses to animals castrated relatively early in life. When animals treated in this way become adults, they do not become sexually active even when treated with massive doses of the appropriate hormones.

TABLE 6. THE EFFECT OF ANDROGEN AND ESTROGEN ON THE MASCULINE AND FEMININE MATING BEHAVIOR OF MALE AND FEMALE ANIMALS *

	Effect on male	Effect on female
Androgen....	Normal masculine response	Sluggish or incomplete masculine response
	Very weak and incomplete feminine response	Sluggish or incomplete feminine response
	Inhibits masculine behavior of castrates if given early in life in large doses	May inhibit feminine responses slightly in intact females
Estrogen.....	Sluggish or incomplete feminine response	Normal feminine response
	Sluggish or incomplete masculine response	Very weak and incomplete masculine response
	May inhibit masculine responses slightly in intact males	Inhibits feminine behavior of castrates if given early in life in large doses

* After Beach, F. A. *Hormones and behavior*. New York: Hoeber, 1948. P. 220. By permission of the publisher.

THE NEURAL BASIS OF SEXUAL BEHAVIOR

We know a good deal about the relation of hormones to sexual behavior, but we do not know exactly how and where they act. On the other hand, we have been collecting a good deal of information about the nervous system and how it functions in sexual behavior. What we know can be divided roughly into two parts: (1) the sensory control and conditions of *arousal* of sexual behavior, and (2) the neuromuscular mechanisms for *executing* mating patterns. We shall consider these two topics now. As we take up the experiments that have been done, we shall try to point out the role of the sex hormones in these neural mechanisms. In the last section we shall have some brief comments about possible physiological theories of sexual behavior.

SENSORY FACTORS

If we analyze the kinds of sensory cues that the male and female animals provide for each other, it becomes obvious that every one of the senses may contribute in one way or another to arousing sexual behavior. There are odors from the secretions of the genital tract of the female rat or dog in heat, the sounds of the "sex calls" of the cat, and the visual cues provided by the reddening of the sexual skin of monkeys or by the courtship behavior of birds. In addition, of course, tactual and kinesthetic cues come into play when the male mounts and grasps the female and when actual contact of the genital organs occurs.

Sensory Deprivation. Much of our knowledge of the importance of these different kinds of stimulation comes from experiments in which mating behavior was studied after different avenues of sensory stimulation were eliminated. In many of the lower vertebrates, we learn, sexual behavior often depends upon one sense modality. Eliminating vision in the frog, for instance, will reduce or eliminate mating (see Beach). Among mammals, however, the case is different. Indeed, no one kind of stimulation is crucial to the arousal of sexual behavior. Male rats mate normally after they have been deprived of vision, olfaction, or hearing. They also mate when surgically deprived of the sense of touch about the snout or ventral body wall and scrotum (Stone). In fact, experienced males will continue to mate until they are made blind, anosmic, and insensitive to touch around the snout (Beach). Inexperienced males, interestingly enough, fail to mate when they have been deprived of any two of these modalities. Results of the same type have been found in the case of the female cat. Removal of the olfactory bulbs and eyes and destruction of the cochlea does not abolish mating behavior (Bard).

Genital Stimulation. Even if sight, sound, and smell are unnecessary for mating behavior, we would expect that the sensory factors in the genital organs might be important. Even that is not the case, however. Female rats show normal mating behavior after removal of the uterus and vagina (Ball). Similarly, in female cats we can interrupt completely both the sensory fibers innervating the sexual apparatus and the sympathetic motor fibers that play a prominent role in its function, and the cats still enter into mating behavior that is normal in every respect (Bard). Similarly, in the male cat we can desensitize the genitalia by sectioning a part of the lower spinal cord, without impairing sexual aggressiveness in any way (Root and Bard). Abdominal sympathectomy in addition to spinal injury abolishes ejaculation but in no way impairs the male cat's sexual activity. In the male hamster, moreover, removal of the seminal vesicles and prostate have no effect on normal mating behavior or on its rate of elimination after castration (Pauker).

Taken together, all these findings indicate that it is the total amount of relevant sensory stimulation rather than any particular kind of stimulation that arouses sexual behavior (Beach). It also looks as if the hormones do not have to sensitize any particular sensory structures. We do know that the sex hormones can induce changes in the nasal membranes (Seward). But it is questionable whether such changes are important in arousing sexual behavior, since anosmic animals mate normally. For any important influence of the hormones we will have to look to the central nervous system.

SUBCORTICAL CENTERS AND PATHWAYS

Physiologists have been hard at work on the problem of the neural mechanisms of mating behavior, and they have given us a good deal of information. It concerns all levels of the nervous system from spinal cord to cerebral cortex.

The Spinal Cord. Certain elementary aspects of sexual behavior are mediated by the spinal cord. In spinal male animals, reflex erection of genital tissue and even ejaculatory responses may be obtained upon mechanical stimulation of the genital regions. Such findings have been obtained in the cat and dog, and the same sorts of reactions can be elicited in spinal human patients even though they are not aware of sensations arising from the genitals (see Bard). In decapitate female cats, stimulating the genital region elicits lateral movement of the tail and treading of the hind feet like that seen in normal animals in heat. Such responses do not depend on estrus, however, for they occur in castrated animals and estrogen does not change them (Bromiley and Bard). One can see similar sexual reflexes in the spinal guinea pig, and they do not depend on sex hormones (Dempsey and Rioch). What these studies show, then, is that certain of the responses typical of masculine and feminine sexual behavior are mediated by the spinal cord. Although sex hormones may influence these reflexes, hormones are not essential—at least, not in the female.

Hypothalamus and Midbrain. Many experiments now tell us that the hypothalamus and midbrain are important in integrating sexual behavior. Ovariectomized guinea pigs, for example, cannot be brought into estrus with estrogen and progesterone unless their diencephalon and midbrain are intact (Dempsey and Rioch). This finding came out of experiments in which guinea pigs were decerebrated at different levels of the brain stem (see page 307). So long as the section passed in front of the mammillary bodies, estrual behavior would follow hormone injection, but if the section passed behind the mammillary bodies it would not. Similar studies in female cats gave the same results.

These results have been confirmed and extended by Bromiley and Bard. Decerebration between the points of exit of the third nerve and the trapezoid body, they found, eliminated estrual responses. Animals decerebrated thus, however, gave certain responses resembling estrual behavior that spinal animals do not show. When their genitals are stimulated, these cats lose extensor rigidity in the forelimbs and assume a posture similar to the estrual crouch of the intact animal. Decerebrated male cats and decerebrated female dogs did not show such responses—they do not normally crouch during sexual activity—but the decerebrate female cat, both in and out of heat, did show them. Taken together, these data point definitely to the posterior hypothalamus and the anterior mesencephalon as the place where estrual mechanisms are activated by gonadal hormones. Centers below the point of exit of the third nerve may integrate more complex aspects of sexual behavior than the spinal levels, but they are not influenced by gonadal hormones.

Localizing Hypothalamic Lesions. Following the leads provided by these studies of decerebration, research workers have looked into the effects of lesions in specific areas within the hypothalamus and midbrain. In one experiment, rather extensive damage in the posterior hypothalamus sometimes abolished estrual behavior in spayed cats injected with estrogen, but sometimes it did not (Bard). Comparing the lesions of affected and unaffected animals leads to the suggestion that including either the anterior mesencephalon or the anterior hypothalamus is crucial. That the latter area is more likely the important one is suggested by several experiments showing the importance of the anterior regions of the hypothalamus in the mating behavior of other animals.

In a study of both male and female rats, lesions in the medial half of the anterior hypothalamus seemed most likely to impair sexual activity (Clark). The crucial areas were not certain, however, for in some cases mating behavior survived this operation. More clear-cut results have been obtained with the guinea pig. In both male and female animals, lesions in the ventral portion of the anterior hypothalamus, between the optic chiasm and the stalk of the pituitary, consistently abolished normal mating behavior (Dey *et al.*, Brookhart and Dey), and injections of gonadal hormones would not bring it out (Brookhart *et al.*). Control experiments made it clear that the effect was due to a lesion in the hypothalamus and not to possible pituitary injury (Dey *et al.*).

We have fairly good evidence, then, that the sex hormones act on the anterior hypothalamus. The data on female rats and guinea pigs fit together very well, and it looks as though the same regions may be important in the female cat. The evidence on male animals is very scanty, but the few cases we do have point to the same areas of the hypothalamus. Below hypothalamic levels, there seem to be centers for the integration of some of the responses that make up the pattern of mating behavior. But these centers apparently do not depend on the action of the sex hormones.

THE CEREBRAL CORTEX

Since most aspects of sexual behavior survive decerebrations above the level of the hypothalamus, one would not expect the cortex to contribute very much to the integration of the behavior. That is how the experiments on females turn out; *e.g.*, the estrual pattern of the cat—which is quite striking—survives complete decortication (Bard). Such is not the case in *male* animals, however. In most male animals that have been studied, extensive cortical lesions definitely interfere with arousal of sexual behavior (see Beach). Among higher animals, furthermore, execution of sexual behavior in male animals is impaired by cortical lesions even when they are not large enough to impair arousal of the behavior.

Female Animals. Despite complete decortication, the female rat, rabbit, cat, and dog readily copulate. In most gross respects the behavior pattern is quite normal, but the organization of the pattern is impaired in some of its finer aspects. On this score we know most about female rats, and there are two points of interest (Beach). First, some of the component parts of copulatory behavior such as ear wiggling, hopping, and lordosis are absent or appear at atypical times in the sequence of responses. Second, any tendency the female has to take the initiative in instigating copulation is eliminated. Decorticate female rats fail, furthermore, to show any of the masculine responses, such as mounting, which occasionally appear in the intact female. Apparently, then, the cortex in infraprimate females is not essential for the arousal and satisfactory execution of the mating pattern. It does, however, play some role in the refinement of the pattern and in the extent to which the female will take an active part in initiating sexual activity.

Male Animals. In male animals the picture is somewhat different. Although complete decortication does not abolish mating behavior in the rabbit, also destroying the olfactory bulbs does eliminate it (Brooks). Apparently copulatory behavior in the male rabbit requires olfactory cues, whereas in the female it does not. If a sizable amount of the neocortex is left intact, however, one may destroy the olfactory bulbs without disturbing mating behavior in the male. Thus it appears that olfactory cues per se are not essential so long as other cues remain available to the animal.

We have available a rather extensive study of the effect of cortical lesions upon sexual behavior in the rat (Beach). It is illustrated in Fig. 145. He found that removal of small portions of the cortex up to about 20 per cent does not abolish copulatory behavior no matter where the lesion is. With more extensive destruction of the cortex, copulatory behavior may or may not be affected, but the larger the lesions, the greater are the number of animals affected. In this connection it is interesting that much larger lesions were required to eliminate sexual behavior in rats that were sexually vigorous before operation than in the less vigorous animals. Conversely, sexual behavior was possible in cases where it had been eliminated by relatively small cortical lesions if sufficient amounts of gonadal hormones were administered. Cortical lesions involving more than about 60 to 75 per cent of the cortex, however, entirely eliminated sexual behavior, and even large doses of sex hormones could not bring it back. From these results, it is clear that the cortex is important in the arousal of sexual behavior in the male rat rather than in its execution.

Evolutionary Status. Cortical lesions have more pronounced effects upon male animals higher than the rat on the phylogenetic scale. In these cases both the arousal and execution of sexual behavior are affected, but to different degrees. While mating behavior in the male cat is possible after unilateral hemidecortication or bilateral removal of any one of the major lobes of the cortex, it is not well integrated (see Beach). Animals prepared in this way often approached the female from the side and began copulatory movements before getting into the proper position. The more of the cortex involved in these operations, the more poorly organized were the attempts at copulation. But interest in the female animals persisted until full decortication was performed.

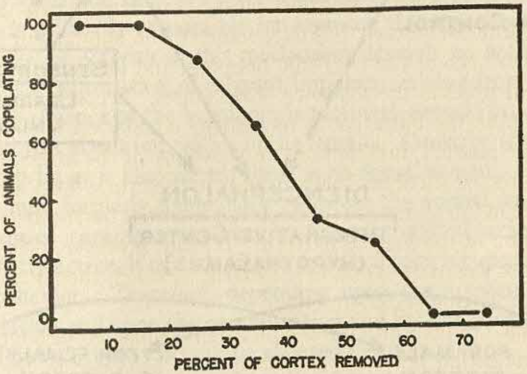


FIG. 145. Relation between extirpation of the cortex and copulatory ability in male rats. (*After F. A. Beach*, 1940.)

No systematic work has been done on the effect of cortical lesions on mating behavior in primates, but we can draw some clear conclusions about the lower animals. (1) The cortex is not essential for copulation in any female animals studied. There is reason to believe, however, that the cortex normally plays a role in the intact female in the ordering of the responses that make up the pattern. In so far as the female initiates mating responses, the cortex may also be important. (2) Sexual behavior survives fairly extensive cortical destruction in male animals, but the arousal of the behavior becomes difficult after lesions involving more than two-thirds of the cortex. (3) The execution of sexual behavior is not impaired in rats that have had the maximal deprivation of cortex that still permits sexual arousal. In cats, however, large cortical lesions disturb motor capacities that are essential in the execution of mating behavior.

Apparently there has been a marked change in the course of evolution in the importance of the cortex in sexual behavior (Beach). This change is reflected not only in the more serious consequences of cortical damage in higher animals, but also in that higher animals can be aroused by a greater variety of stimuli and can exhibit more variable patterns of sexual behavior than lower animals.

Furthermore, animals that stand high on the phylogenetic scale depend far less upon the gonadal hormones for the arousal of sexual behavior than do lower animals. These developments reach their high point in man, who depends far less on gonadal hormones than any other animals and who is aroused by a wider variety of stimuli and shows a much more variable pattern of sexual behavior.

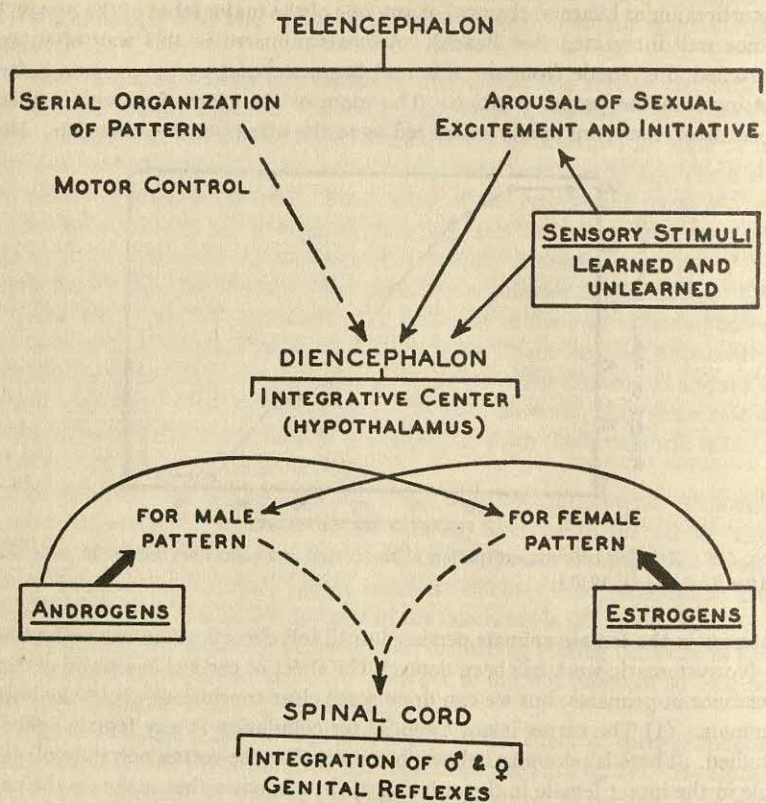

TELENCEPHALON
SERIAL ORGANIZATION OF PATTERN
AROUSAL OF SEXUAL EXCITEMENT AND INITIATIVE
MOTOR CONTROL
SENSORY STIMULI
LEARNED AND UNLEARNED
DIENCEPHALON
INTEGRATIVE CENTER (HYPOTHALAMUS)
FOR MALE PATTERN
FOR FEMALE PATTERN
ANDROGENS
ESTROGENS
SPINAL CORD
INTEGRATION OF ♂ & ♀ GENITAL REFLEXES

FIG. 146. Schematic diagram of the hormonal and neural factors in the regulation of sexual behavior. Solid arrows indicate the factors important in the arousal, and dotted arrows those important in the execution, of sexual behavior.

PHYSIOLOGICAL THEORY OF SEXUAL BEHAVIOR

The evidence we have been viewing goes a long way toward giving us an understanding of the mechanisms that regulate sexual behavior (see Fig. 146). On the physiological side there are two main mechanisms, the hormones and the nervous system. On the behavioral side, the two main problems to be understood are the arousal and execution of mating behavior. The nervous mechanisms are the fundamental ones in the execution of sexual behavior and the hormones are of only secondary importance. But both the nervous system and the hormones operate in the arousal of the behavioral pattern. The task of a physiological theory of sexual behavior is to account for the way in which the hormonal and neural influences combine in the control of the arousal and execution of sexual behavior.

Arousal of Mating Behavior. Beach has presented a well-integrated scheme of the neuroendocrine relationships in the regulation of sexual behavior. The essence of his view is that there is a central excitatory mechanism in the nervous system which is primarily responsible for arousing the organism to sexual activity. The level of activity of this mechanism depends on both the gonadal hormones and the summation of afferent impulses arriving from the receptor organs. If the influence of the hormones is removed, arousal becomes difficult in the male and just about impossible in the female. Similarly, if enough of the relevant sensory input is eliminated, there is no sexual arousal. On the other hand, new stimuli, formerly inadequate to arouse the animal, can become effective by virtue of learning or experience. Once the central excitatory mechanism is sufficiently active, it can set off the neural circuits integrating masculine or feminine behavior. Therefore, depending upon the amount and kind of sensory stimulation and upon the concentration and kind of gonadal hormones, masculine or feminine behavior will be aroused in an animal.

Hypothalamus. We may assume that sexual arousal depends upon the level of excitation of the hypothalamic centers known to be important in sexual behavior (see Fig. 146). We know, for example, that sexual arousal is impossible in the absence of these centers, even though many of the component responses that make up the sexual pattern are integrated at bulbar and spinal levels. Furthermore, it is clear that one of the most important effects of the gonadal hormones is to arouse activity in the hypothalamic centers. Other influences that are important in sexual arousal may well exert their effects through the hypothalamus.

Cortex. It is entirely possible that afferent impulses arising from sensory stimulation may influence the excitability of the hypothalamus, either directly or through the cortex. Or the cortex itself may contribute to the excitation of the hypothalamus, as it apparently does in the case of sleep and wakefulness. In all likelihood, the contributions of the hormonal, sensory, and cortical influences are additive, for in many cases it is possible to compensate for the absence of one of these factors by increasing the contribution of the others. Thus we have seen that when the arousal of sexual behavior is impaired by cortical damage, gonadal hormones may restore it. Similarly, in higher animals, which presumably have a greater cortical contribution and have learned to be aroused by a wide variety of stimuli, the hormones are not always essential for sexual behavior. The important thing for a hypothalamic theory of sexual behavior is simply that the hypothalamic centers be activated. Whether the activation arises from one set of afferent impulses or another, male or female gonadal hormones, the cortex, or some combination of these influences, is not important for the arousal of sexual behavior.

Execution of Mating Behavior. As for the execution of mating behavior, we can believe that the hypothalamus is also the most important single integrating center (see Fig. 146). Spinal or bulbar animals show only fragments of the complete pattern, but decerebrates with their hypothalamus intact give a more nearly complete pattern. The cortex normally plays a role in the integration of mating, but it is mainly concerned in the organization of the separate responses into a consistent sequence. In addition, of course, the cortex is important in higher animals for maintaining satisfactory motor control.

Comment. Using this schematic view, it is possible to understand some of the evolutionary changes that have taken place in the regulation of sexual behavior in physiological terms. Among the lower animals, only the gonadal hormones and the afferent impulses operate to control the activity of the hypothalamic centers. The higher an animal is on the phylogenetic scale, however, the more likely it is that it will learn to be aroused by new stimuli that were originally inadequate to elicit sexual behavior, therefore the more it will become independent of hormonal influences. Finally, the more highly developed the cortex of an animal, the more it will contribute to hypothalamic excitability, and in such cases it may be possible to do without hormonal influences entirely. At the same time, however, such animals are more readily affected by damage to cortical tissue than are lower animals.

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CHAPTER XXI

CONDITIONING

Conditioning, the subject of this chapter, is a hard word to define. Fifty years ago, when conditioning was 'discovered,' it could be defined in terms of the procedures that produced it. Pavlov, its 'discoverer,' had three essential steps in his procedure. First was the presentation of food to a hungry dog. This food he called the unconditioned stimulus, for it brought about a response of salivation on the part of the dog without any prior conditioning or learning. The second step was to ring a bell a few seconds before the presentation of food and to repeat the sequence several times each day for several days. This was the essential step in the conditioning procedure. The final step was to ring the bell without presenting the food and to measure the saliva that flowed in response to the bell alone. If these three steps were carried out properly, there would be a salivary response to the sounding bell—this was conditioning—brought about by the repeated pairing of the bell and food.

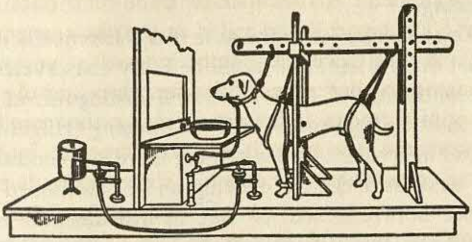

FIG. 147. Pavlov's method of establishing a conditioned salivary reflex. Food, the unconditioned stimulus, is presented automatically through the window. Just before the food is presented, the conditioning stimulus, a bell, is sounded. After the sequence, bell–food, has occurred a good many times, the dog comes to salivate when only the bell sounds. Saliva from the dog's jowl flows through a tube, and each drop hits a lever that makes an automatic tracing on the smoked drum behind the screen. In this way a record of the conditioned response, *i.e.*, salivation, is made throughout the course of conditioning. (*From R. M. Yerkes and S. Morgulis. The method of Pavlov in animal psychology, p.* 264. *Psychol. Bull.*, 1909, 6, 257–273. *By permission of the American Psychological Association.*)

Classic Conditioning. Such was the classic procedure for conditioning (see Fig. 147). There was always an *unconditioned stimulus* which, before any learning, would evoke some relatively specific response. The essential feature of the conditioning was that some neutral stimulus, the conditioned or *conditioning stimulus*, could come to evoke the specific *unconditioned response* if the stimulus was paired with the primary unconditioned stimulus. Today this kind of conditioning is called *classic* or *substitutive conditioning.*

By degrees, however, the notion of conditioning has been broadened since Pavlov's day. Theorists, in their search for a basic understanding of complex learning, have supposed that classic conditioning was the paradigm for all learning, that it could be used to explain the most complex of learning and thought processes (Hilgard, Hull). That was one factor making for a loose use of the term conditioning in all sorts of learning. Another was the development of many new and varied conditioning procedures. Today there are dozens of ways in which to study learning phenomena in animals. These various procedures have their similarities and their differences. The simplest procedures are very similar to the original classic conditioning of Pavlov; the more complex procedures are more akin to reasoning problems for college students. Experimenters have had a hard time drawing the line at any particular place; instead they have tended to call a great variety of these procedures 'conditioning.'

Instrumental Conditioning. For the sake of a coherent discussion and interpretation we must draw a line, but it will be fairly conservative. In addition to the classic conditioning of Pavlov, we will distinguish another relatively simple type of conditioning, *instrumental conditioning* (Hilgard and Marquis). In both classic and instrumental conditioning there is a conditioning stimulus, which comes to serve as a cue for evoking an unconditioned response. The essential difference between them is that in instrumental conditioning the response of the subject does something to the unconditioned stimulus, usually preventing it or allowing the animal to escape it—thus the term 'instrumental.' The best example of the instrumental conditioning situation is conditioning an animal to lift its leg or to run to avoid or escape an electric shock when a light or bell (the conditioned stimulus) is turned on. The animal responds to the signal by doing something to get away from the unwanted unconditioned stimulus.

Those are the two kinds of conditioning we shall deal with in this chapter. Other kinds of learning which have sometimes been called conditioning will be considered in a subsequent chapter on problem-solving. This kind of grouping is somewhat arbitrary, for instrumental conditioning certainly has much in common with problem solving. Indeed, we can be quite sure nowadays that there are not separate kinds or classes of learning. The separation, however, is a good one for our purposes.

SPINAL CONDITIONING

We shall lead off with a very basic but debatable question. What is the lowest level of the nervous system in which we can find conditioning? We cannot give a definite answer to this question at present, but the story of what we know and do not know about conditioning in the nervous system will show you what progress we are making with the question and where research must be directed in the future.

Conditioning of the Nervous System. We know, of course, that the ability of man and the higher animals to acquire complex habits is correlated with a tremendous development of the cerebral cortex of the brain. So impressive is this correlation that many in the past, both scientists and laymen, have been inclined to believe that it is the cerebral cortex that is responsible for all our learning ability. Pavlov, the discoverer of the conditioned reaction, thought so, and so have many others.

On the other hand, if we take a quick glance at lower animals, we see that they can learn even though they have no cortex. The fishes with no true cortex learn simple conditioned reactions perfectly well (Schiller). Indeed, insects and invertebrate animals, which do not even have a brain, are capable of learned reactions (Maier and Schneirla). And there is even some evidence of simple conditioning in such unicellular animals as the paramecium, which do not even have a nervous system (see Maier and Schneirla). All this leads us to believe that learning and conditioning, in their simplest forms, are basic properties of the lowest and most primitive nervous elements. Indeed, in the vertebrate and mammalian animals we might expect to find the spinal cord, the lowest level of the nervous system, capable of conditioning. A few investigators have therefore made a search for conditioning in the spinal cord.

Studies of Spinal Conditioning. The search began with a study of the spinal rat (Prosser and Hunter). In this animal, however, nothing deserving the name 'conditioning' could be found in spinal preparations. If the unconditioned response, a leg lift, was elicited often enough by electric shock, there was some adaptation of the responses, but this could not be called conditioning. The search has been continued, however, by two other groups of investigators, one headed by Kellogg, the other by Shurrager. Unfortunately, one group has reported affirmative results, the other negative results. The two groups, however, have used rather different techniques, and it is quite likely that the techniques have something to do with the results. We shall therefore consider both the techniques and the results of both research workers.

TECHNIQUES

The kinds of techniques used in spinal conditioning and the differences between them will be brought out if we simply describe in turn the techniques that have been employed by Shurrager and Kellogg, respectively (see Fig. 148).

The Shurrager Technique. This procedure was developed earlier by Culler and his collaborators for studying all sorts of conditioning problems in which a very sensitive response was desired. It requires special surgical procedures to prepare the muscle to be used in the unconditioned response. The ***semi-***

tendinosus muscle, a muscle of the hind limb of the dog, is dissected out, taking care to keep the blood and nerve supply intact so that the muscle can respond reflexly to unconditioned stimuli. Twitches in this nerve-muscle preparation are noted and recorded either by watching the muscle with the naked eye or by attaching to the muscle a recording stylus which will make a mark on a rotating drum whenever the muscle twitches. In this way extremely small reactions, involving probably only one neuromuscular unit (see page 274), can be observed.

The unconditioned stimulus for the muscle twitch, in Shurrager's experiments, has been an electric shock applied to the foot pad of the same limb from which the semitendinosus muscle was dissected. Because the muscle is a flexor muscle, it gives a reflex response to the noxious stimulus of the electric shock of the foot pad. For a conditioning stimulus, Shurrager has used either gentle pressure or a weak electric shock to the tail of the dog. Thus, when conditioning occurs through repeated presentations, the tail stimulus comes to evoke the same muscle twitch originally brought out by the electric shock on the foot pad.

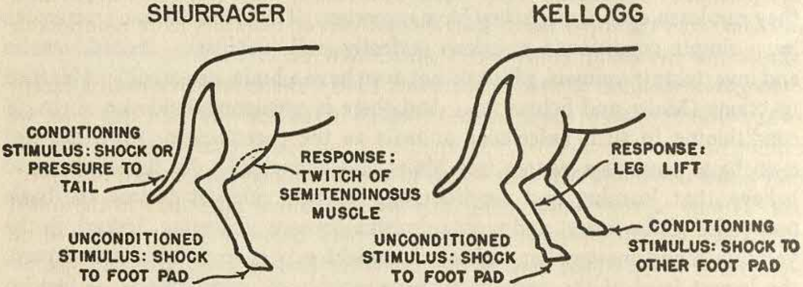
SHURRAGER
KELLOGG
CONDITIONING STIMULUS: SHOCK OR PRESSURE TO TAIL
RESPONSE: TWITCH OF SEMITENDINOSUS MUSCLE
UNCONDITIONED STIMULUS: SHOCK TO FOOT PAD
RESPONSE: LEG LIFT
UNCONDITIONED STIMULUS: SHOCK TO FOOT PAD
CONDITIONING STIMULUS: SHOCK TO OTHER FOOT PAD

FIG. 148. Diagram of the techniques for spinal conditioning used by Shurrager and by Kellogg. They differ in the conditioning stimulus used: in one case it was to the tail and in the other to the opposite leg. They also differ in the response: in one case it was a twitch of the semitendinosus muscle (dissected out) and in the other a lift of the whole leg.

To see whether conditioning of this sort can be obtained in the spinal dog the spinal cord must, of course, be transected before the beginning of the experiments. This was done by a cut in the lumbar region of the spinal cord. Although 'spinal' animals prepared in this way can sometimes be kept in healthy conditions for long periods of time, Shurrager always used "acute" preparations, *i.e.*, he did all the experiments within a few hours after the spinal operation, and he did not attempt to maintain his animals in that condition for long periods of time.

Kellogg's Technique. The procedures of Kellogg are different in several respects. In the first place, he has used only chronic preparations—dogs whose spinal cords had been transected and who had survived the operation almost indefinitely. Also, instead of using the muscle twitch of a single muscle, he observed the flexor response of the whole leg. His unconditioned stimulus was the same as Shurrager's—an electric shock to the foot pad of the same leg—but his conditioning stimulus was different. It was a shock applied to the opposite hind limb of the animal rather than a stimulus on the tail.

RESULTS

With these different procedures, the two groups of investigators have come out with different results. Shurrager and his colleagues have reported that spinal conditioning takes place. We shall consider his results in detail in a moment. On the other hand, Kellogg and his collaborators have been unable to measure any conditioning with their procedures.

Negative Results. There is not much to say about negative results except to say that they were negative and then go on to ask why. In this case, we cannot be sure why Kellogg was unable to find spinal conditioning. We can only point out the possibilities which in the future may be affirmed or denied.

1. It may be that conditioning does not and cannot take place in the spinal cord and that all Shurrager's results, described below, must be explained on some other basis. That may be the reason for Kellogg's negative findings.
2. It is possible that conditioning does take place but to such a small extent and under such refined conditions that it cannot be seen in the total leg lift of the dog used by Kellogg and can only be seen in the muscle-twitch technique of Shurrager.
3. It is possible that conditioning can take place, but that Kellogg could not observe it because of the particular type of conditioning stimulus he used. Note that he employed a shock to the limb opposite the one responding to the unconditioned stimulus. Back in an earlier chapter (page 301) we saw that a noxious stimulus to one leg can produce a crossed extension reaction. Such a reaction would be exactly the opposite of the flexion response called out by the unconditioned stimulus. It is possible that any conditioning of the flexion response that might have occurred was canceled out by crossed extension reactions to the conditioning stimulus.

Positive Results. Shurrager, as we said, obtained positive results. For some reason not explained at present, he got them in only 98 of 219 different dogs used in the experiments. In those dogs that were conditioned, the conditioning took place in 20 to 120 trials and the average rate of conditioning was 51 trials. This 'spinal conditioning,' like the classic conditioning of Pavlov, could be extinguished by presenting the tail stimulus (conditioning stimulus) repeatedly without reinforcement from the foot-pad stimulus (unconditioned stimulus). On the surface, at least, these results look like spinal conditioning. This report of spinal conditioning is remarkable. Even more interesting, however, are some of the other phenomena of spinal conditioning that Shurrager reports.

Rate of Conditioning. One of these is the rate at which successive conditionings and extinctions proceed (Shurrager and Culler). In Fig. 149 you see a series of conditioning and extinction curves. You will note that the first time the dog is conditioned, the curve of increasing conditioned responses proceeds relatively slowly. Extinction, too, following the first conditioning goes relatively slowly. If the dog is reconditioned, however, the conditioning proceeds more rapidly than it did the first time; so also does the second extinction. Likewise, the rate of conditioning and extinction on the third and fourth series is even faster than in the first and second.

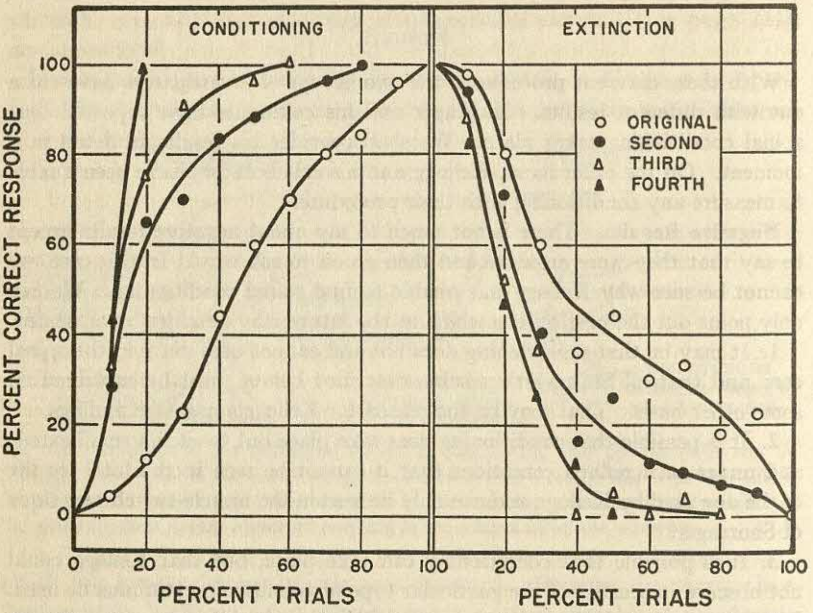

FIG. 149. Rate of conditioning and extinction in experiments with spinal animals. Conditioning and extinction were repeated four times in this experiment. Each time the rate was faster than the time before. (*After Shurrager and Culler*, 1940.)

Extinction of a Reflex. Another remarkable aspect of Shurrager's work is the report that a normal unconditioned reflex, one that is 'built into' the spinal cord, so to speak, may be permanently extinguished by a conditioning procedure (Shurrager and Shurrager). The procedure demonstrating this phenomenon was to prepare the semitendinosus muscle in both hind limbs of the dog. In some dogs the muscle on one side—let us say, left—would 'naturally' respond to the tail stimulus. This same stimulus, of course, is the one used as a conditioning stimulus for conditioning the muscle of the other leg (right). During the course of the conditioning, Shurrager reports, the reflex response of the left leg to the tail stimulus disappeared and stayed that way. In a word, then, the normal reflex on one side was extinguished during the course of conditioning the flexor reflex on the other side.

Conversion of a Conditioned Reaction. A third phenomenon reported by Shurrager is that a conditioned reaction of a semitendinosus muscle twitch can be converted into a permanent reaction—what looks like a normal unlearned reflex—by cutting the dorsal (sensory) roots of the spinal cord on the side *opposite* the conditioned muscle reaction. Even though the phenomenon involves surgical procedures, such a conversion of a learned reaction into a so-called *normal* reflex is a remarkable and unexpected result.

Conditioning of the Single Synapse. Finally, Shurrager reports what he believes to be conditioning taking place at a single synapse of the spinal cord. In the early stages of conditioning, extremely small all-or-none twitches of the semitendinosus muscle can be observed. Such all-or-none responses would seem to represent the response of a single neuromuscular unit—one neuron and the muscle fibers that it serves. When the form of the learning curve for such all-or-none conditioned responses is plotted, it takes the form of a straight line. From this fact, Shurrager suggests that the 'true' or basic learning curve is a straight line and that all other forms of learning curves—usually curvilinear—seen in other learning experiments are due to the compounding of several synaptical units participating in learning.

Interpretation. What these results mean is something upon which physiological psychologists are not agreed. Unfortunately, Shurrager did not carry out some of the controls needed to make a final interpretation. For example, from his reporting of the 'extinction' of a spinal reflex we might suspect that there is an *unconditioned* response of the semitendinosus muscle to tail shock. It was Deese and Kellogg, however, who proved the point by testing for semitendinosus responses to tail shock without reinforcement with big shocks.

Moreover, in noting that successive conditionings and extinctions were increasingly more rapid, Shurrager did not test whether this would have been the case irrespective of the number of shocks given the animal. It is quite possible that the so-called spinal conditioning is not the result of pairing the tail stimulus with the foot-pad stimulus but is just the result of giving the animal so many shocks on the foot. There is evidence in other physiological experiments that the presence or absence of a response (in this case, to the tail stimulus) can depend on how much shock is administered. If such were the case, we should think of reflex sensitization rather than of spinal conditioning (see Kellogg *et al.*).

The suspicion that this may be the correct interpretation is strengthened by the phenomenon of conversion of the conditioned reflex into a permanent reflex. This phenomenon, you will remember, occurred because the tail stimulus, normally used as a conditioning stimulus, could in some animals bring out the muscle twitch without any prior conditioning at all. This fact makes one believe that the so-called unconditioned tail stimulus actually had reflex connections with the semitendinosus muscle which might be strengthened or weakened by applying shock to the animal or allowing the animal a rest from shock.

Finally, in reporting the conversion of the conditioned reaction into a permanent reaction by cutting the contralateral dorsal roots, Shurrager does not tell us of any control experiment—an experiment to see whether such severing of the roots might have produced the change without any preceding conditioning procedure. Bromiley, however, has done the control experiment and tells us that the so-called conversion can take place without any conditioning procedure.

So there is a good deal wrong with the experiments as they stand. They do not let us conclude confidently that spinal conditioning can take place. We need more experimenting before we can be sure. In fact, it may turn out that what seemed to be conditioning is more correctly called reflex sensitization, as Kellogg has suggested above. Even if that is the case the experiments will be of some value, for knowing as little as we do about conditioning, it is possible that conditioning may be closely related to reflex sensitization.

DECORTICATE CONDITIONING

If we could, we would proceed through the nervous system in an orderly manner, taking successively higher levels of the nervous system to consider their role in conditioning. Unfortunately, however, we are limited by the research that has been done, rather than what we would like to see done. And in the case of conditioning there is no work, so to speak, between the spinal cord and the cerebral cortex. We have no studies of conditioning in decerebrates, which might tell us what the medulla, the midbrain, or the thalamus do in conditioning. We must jump, therefore, to the level of the cortex and ask what function it performs in conditioning.

Early Work. Back in 1911, Zeliony, a Russian colleague of Pavlov, first attempted to study conditioning in the totally decorticate dog—a dog deprived of all neocortex (see page 57). Zeliony failed. His failure caused Pavlov and many others interested in conditioning behavior to believe that conditioning was solely the property of the cerebral cortex. Many years later, in 1930, however, Poltyrew and Zeliony repeated the early attempts. This time they succeeded in obtaining conditioned responses in decorticates (dogs). In fact, in two of the animals a rather sophisticated type of conditioning could be obtained; the animals learned to lift one forepaw (to avoid shock) to the sound of a whistle and the other forepaw to the sound of a knock on wood.

These positive results with decorticate conditioning reopened the whole question for American investigators. The Russian research workers, however, had not reported any post-mortem checks of their animals to prove with certainty that their animals were in fact decorticate. The decortication of an animal is a tricky affair. It is hard to be sure at the time of operation that complete decortication is really achieved. That was one reason for repeating the Russian work. Another was to look into the question of whether, if conditioning occurs in decorticate animals, it differs in any way from the rate and pattern of conditioning in normal or incompletely decorticate animals.

Adaptive vs. Diffuse Patterns. In the later American research, bolstered by adequate post-mortem examinations of the subjects' brains, there is no question about conditioning occurring in decorticate dogs. Several investigators (Culler and Finch; Girden *et al.*; Bromiley) have obtained conditioning. They all have used the instrumental type of conditioning—training an animal to lift a paw to avoid shock when presented with a warning signal. Auditory signals, thermal stimuli, and tactile stimuli have all been successfully employed in decorticate conditioning. Thus is dispelled the notion that learning or conditioning depends upon the cerebral cortex. We know that some subcortical centers, as yet undetermined, can carry on conditioning processes.

Diffuse Conditioning. A new problem, however, has developed. How do conditioned responses in decorticates differ from those in normal animals? To Culler and his collaborators it appeared that there might be a difference in the diffuseness vs. the specificity of the conditioned response. The normal conditioning of a dog to flex its paw ordinarily goes through two stages (Girden *et al.*). In the first there is a diffuse conditioned reaction to the conditioning stimulus, *e.g.*, a bell; the animal squirms, squeals, and makes a host of uncoordinated movements when the bell sounds, just as he would when first shocked on the paw. The second stage has been called 'adaptive' conditioning; the animal leaves out all the unnecessary squealing and squirming and calmly raises its paw—the specific adaptive response that lets him avoid the shock. It is this second stage that Culler and his colleagues thought was absent in the conditioning of the decorticate. At least they did not observe it in the two completely decorticate animals that they studied. They saw only the diffuse conditioned reactions. They therefore concluded that specific adaptive conditioned responses depend on the cerebral cortex, but that diffuse conditioning can take place subcortically.

Adaptive Conditioning. Apparently, however, this conclusion is not true—at least it is not always true. A more recent study with a dog, whose practically complete decortication is not in doubt, demonstrated that adaptive conditioned reactions can be obtained in decorticate animals (Bromiley). In this study, by taking great pains not to shock the dog when it was disturbed, specific flexure of the front paw could be conditioned to the sound of the bell. Moreover, a differential discrimination could be built up; by appropriate training, the animal could learn to raise its paw to a light stimulus and not to respond to the bell stimulus. This study is a sound one, and even though the distinction between diffuse and adaptive conditioning is an attractive one, we cannot say that this is a true distinction to be made for the decorticate animal.

This story might sound as though different investigators have been getting contradictory results. Actually, if we went into the details of procedure in each of the experiments, they would not seem so contradictory. Decorticate animals, as we saw several chapters ago in the study of emotions, are very emotional animals. They are freed of many of their inhibitions and their complete perceptual mechanisms. They therefore are easily disturbed. They snarl, squirm, and get excited more easily than normal animals. Thus the diffuse emotional aspects of their behavior are much more prominent than in normal animals, and it is consequently more difficult to get them to settle down for a session of conditioning involving the application of a noxious stimulus, such as shock. It is therefore fair to say that this diffuse behavior can interfere with adaptive behavior more easily than in normal animals, even though, by taking great care, the animals can be taught an adaptive conditioned response.

Obviously, there must be some other differences between decorticate and normal conditioning, which would be found if we varied the kinds of experiments enough to see what the limits of conditioning ability are. We must await future research in this area, however, to give us the complete picture of these differences, for we do not have it at the present time.

DISSOCIATION OF CONDITIONING UNDER CURARE

In a moment we shall come to the cortex and the role of specific areas of the cortex in conditioning. Before we do, however, there is a story to tell about conditioning experiments with a drug called curare. This drug, because of its peculiar physiological properties, happens to produce some unusual phenomena in conditioning. These phenomena throw some light on the functioning of cortical and subcortical centers in conditioning. That is our reason for telling the story.

The Curare Drug. Curare was the poison used by Indians on arrowheads and prepared by extraction of various poisonous plants. It is not a pure drug, and it varies a great deal in strength and purity. The active ingredient, curarine, is an alkaloidal compound with an approximate formula of $C_{19}N_{21}NO_4$. Because the impurity of curare gives varying results in experiments, sometimes underdosing the animal, sometimes killing it, investigators have sought other substitute materials. Recently the drug *erythroidine* has been prepared in relatively pure form. Although it is not identical with curarine, it has the same physiological properties. Thus experiments in the 1930's used curare, but those in the last few years have employed erythroidine.

Conditioning Techniques. The outstanding property of these drugs, known for a long time, is that they produce muscular paralysis without appreciably affecting sensory functions. Physiological experiments have indicated that the site of action of the drugs is at the neuromuscular juncture. Curare seems to produce its paralytic effects by blocking the transmission of impulses from the motor axon to the muscle fibers. It is this property that first prompted its use by psychologists (Harlow and Stagner). They wanted to use it as a means of paralyzing an animal during conditioning to see whether it is necessary for responses actually to occur in order for conditioning to take place (see page 454). In these experiments they gave conditioning training to animals under the influence of curare and tested them for conditioning after the curare had worn off. They found no conditioning. They concluded that "conditioned reflexes are only possible if a response is made, and do not result merely from stimuli presented simultaneously."

A few years later it was to become clear why this result had been obtained. Girden and Culler devised a new technique for studying conditioning under curare. This was the technique already described above in connection with spinal conditioning, in which the semitendinosus muscle is dissected out, keeping the blood and nerve supply intact. When they applied shock to the hind leg, they could observe muscle contractions in the dissected muscle, even though gross flexor responses of the limbs did not occur. By pairing the sound of a bell with the application of a shock, they were able to observe conditioning taking place in the semitendinosus under curare. In a series of studies, thereafter, they used this technique in both normal and curarized animals to observe the course of conditioning and of retention in both normal and curarized states.

Dissociation. The most interesting point—the main point of this section—is that the responses conditioned under curare vanished when the animal was returned to the normal state. The normal animal showed no sign of retention of the conditioning that had taken place under curare. Conversely, conditioning that was established in the normal animal disappeared when the animal was put under curare. Thus there was a complete amnesia in one state for conditioning in the other state. This fact has now been repeated many times, and there can be no doubt about it (Culler *et al.;* Girden).

Once the dissociation of skeletal conditioning in normal and curarized animals had been established, the investigators went on to see whether the same rule also held for autonomic responses. It was easy to show that pupillary conditioned response to bells could be established under curare (Harlow; Harlow and Settlage). Preliminary experiments also seemed to indicate that there was no dissociation of such conditioned autonomic reactions in the normal and curarized state (Harlow and Stagner). Later, however, in more thorough research, it appeared that apparent carry-over of the conditioning of pupillary reactions from the curarized to the normal state was an artifact. Specifically, it looked as though the pupillary reactions under curare were actually unconditioned reactions to the bell which was being used presumably as a conditioning stimulus. At any rate, when a light was used instead of a bell for conditioning pupillary dilation, there was a dissociation of conditioning like that seen in the skeletal responses of the semitendinosus muscle.

This finding has been established with the use of both curare and erythroidine (Girden). Moreover, experiments with other types of autonomic responses, such as conditioned reactions of change in blood pressure to shock, show a clear dissociation between the normal and the curarized state (Girden). Thus the story now seems to be simple and clear. Conditioned reactions, whether skeletal or autonomic, established under curare or erythroidine do not carry over to the normal state, and vice versa.

Equivalence. The next question is the physiological interpretation of these effects. That comes from a study of the effects of curare upon different parts of the nervous system. Culler and his collaborators, suspecting that the curare was doing more to the nervous system than simply paralyzing neuromuscular transmission, examined the excitability of the cerebral cortex and the spinal reflex paths in normal and curarized states. They found that for the threshold, the time for excitation as well as evoking responses in the semitendinosus muscle by cortical stimulation, was depressed. In a word, the excitability of the motor cortex, and probably of the cortex as a whole, was considerably depressed. By stimulating the motor roots of the spinal cord leading to the semitendinosus muscle, it was clear that curare had not changed the excitability of the neuromuscular response. At first thought this might seem to contradict the idea of curare paralyzing neuromuscular junctures. It does not, however, because it turns out that curare does paralyze many of these junctures; on the other hand, it seems to sensitize some of the fibers not knocked out. The end result is no change in excitability.

The conclusion, then, from these electrophysiological studies is that curare considerably depressed cortical excitability but did not affect spinal excitability. This suggests that the dissociation of conditioning seen in curarization is due to a depression of the cortex. Going further, one might conclude that normal conditioning involves the cerebral cortex, while conditioning under curare, with accompanying depression of the cortex, is effected through subcortical routes. This subcortical conditioning, then, gets suppressed when the cortex returns to normal.

Role of Auditory Cortex. This hypothesis has been tested and confirmed. Girden, because he was using a bell as the conditioning stimulus, removed the auditory cortex of dogs before conducting the typical experiments with curare. According to the hypothesis above, the auditory cortex, in addition perhaps to other cortical structures, would be involved in the normal state but would be suppressed in curarization. If, however, *it were removed*, then it could not function in either the normal or the drugged state. All conditioning, whether normal or under drugs, would then be subcortical, at least with respect to the bell stimulus. One would *not* expect dissociation under these conditions, and there was none. The conditioned response of the semitendinosus muscle established in either the normal or the drugged state carried over to the other state.

The conclusion to the story now seems rather clear. In conditioning skeletal and autonomic reactions in normal animals, the cortex is involved—at least in bell-shock conditioning. Under the drug, which depresses the cortex, leaving subcortical centers at some level more or less unaffected, conditioning takes place subcortically. There is a dissociation between these two conditionings. The cortex and subcortex are alternates for each other—they are equivalent—but not at the same time. When one is working the other is not, and vice versa.

There may turn out to be some errors in this interpretation, but so far it looks like the best one for the case of auditory conditioning in normal and curarized states. To carry the interpretation over to any other kind of conditioning, say light-shock conditioning, is a bit hazardous, however, for there seem to be some marked differences in the role of the auditory and visual cortices in conditioning. We shall come to these in the next section of the chapter.

CORTICAL AREAS IN CONDITIONING

We have talked so far about conditioning that occurs in the absence of the brain or of the cerebral cortex. The next thing, logically, is to consider the cortex itself and to tell what we know about different parts of the cortex in conditioning processes. That will be the order of business in this section. As a matter of convenience we shall divide the material according to the techniques of conditioning, whether classic or instrumental.

Classic Conditioning

Actually, there are relatively few studies of conditioning of any type in which the effect of particular areas has been considered, and there is only one such study of classic conditioning. This is the conditioned eyewink in the dog (Marquis). A puff of air on the eyeball was the unconditioned stimulus for eliciting the eyewink. The flash of a light was the conditioning signal. In the normal dog, a conditioned reaction of the eyewink to the light builds up rather quickly. So it does, too, in animals with lesions in the cerebral cortex.

Of course, you would not expect areas other than the occipital area of the cortex to have anything to do with a visual conditioned reaction. Even this, however, makes no difference. Dogs without the visual cortex acquire the conditioned reaction in just about the same time as normal dogs. Moreover, removal of the visual cortex after the conditioned reaction has been acquired does not disturb the conditioned reaction. Putting all these facts together, it looks as though the classic conditioning of the eyewink to light does not normally involve the cerebral cortex but rather depends upon subcortical centers of the visual system. This may seem very logical and as it should be, but in some of the studies of visual discrimination and auditory conditioning that we will take up later, you will see that the situation is not nearly so simple.

INSTRUMENTAL CONDITIONING

Conditioning of the instrumental type is now familiar to you. The animal is presented with a shock, which he can escape by lifting his foot. Shortly before the shock a signal, the conditioning stimulus, comes on, and if the animal learns to respond to this by lifting his foot, he can escape shock altogether. The studies to be taken up here used that technique.

Visual Conditioning. The story for instrumental visual conditioning is much the same as that for classic visual conditioning, which we have just described. Animals lacking their visual cortex are perfectly capable of learning to lift their leg when a light is flashed on as the signal (Wing and Smith). The experiments, however, have been carried further than that. A light can be left on all during the experiment but changed slightly in intensity just before the shock comes on (Wing). Dogs without the striate cortex can use this change in the intensity of the light as a conditioned stimulus for leg retraction. Finally, by a slight change in procedure so that an animal is rewarded by food instead of avoiding shock for lifting its leg, the same thing can be demonstrated with a reward type of instrumental conditioning (Wing). In a word, then, animals do not need their visual cortex to learn simple and differential instrumental conditioning to a visual stimulus.

There is still another question which, as you will see, becomes quite important in complex types of learning. Even if a cortical area is not necessary for learning, does its removal disturb the retention of conditioning that has already taken place? In the case of the classic conditioning of the eyewink, the removal of the visual cortex has no effect on retention. Neither does such removal affect retention of the simple and differential conditioning to a visual stimulus described above (Wing). We can say, then, that the visual cortex is involved neither in the original conditioning nor in the retention of visual conditioned reactions. So we may presume that such conditioning is carried out entirely by subcortical centers.

Auditory Conditioning. For some reason we meet a different sort of story in instrumental conditioning to an auditory stimulus such as a bell (Raab and Ades). Here there is a real distinction between original conditioning and retention. Just as in visual conditioning, we find that a dog learns a conditioned leg lift to a bell when the auditory cortex is completely removed on both sides. Apparently, therefore, the auditory cortex is not necessary. If, however, the auditory cortex is removed after the conditioning occurs—in this case, the experiment was on cats—there is a complete amnesia for the conditioning, and training has to be carried out all over again before the conditioned response is relearned.

This is a curious state of affairs, which we shall meet with repeatedly in later pages. It makes us come to the conclusion that the

> auditory conditioned responses are normally mediated cortically by an all-or-none mechanism of the auditory cortex. In the absence of the projection areas, these habits may be relearned at a midbrain level and are mediated by the inferior colliculi (discharging through the superior colliculi) with no loss of acuity.[1]

In a word, these studies point to an equivalence of cortical and subcortical centers in auditory conditioning; when the cortex is intact, it is crucial to the learning; when it is not, subcortical centers mediate the learning.

We cannot be sure why there is this difference between visual conditioning and auditory conditioning. When practically identical instrumental conditioning techniques are employed, removal of the visual cortex has no effect on retention of visual conditioning, whereas removal of the auditory cortex destroys the auditory conditioning habit. There are one or two suggestions for accounting for the difference, but these will be offered later in the chapter on discriminative learning, where the general problem of equivalence of nervous structures is thoroughly considered.

Comment. You will note that none of the experiments we have been talking about make use of the maps of sensory areas gotten by the method of evoked potentials. This method, as we have seen in earlier chapters, always gives us two areas (I and II) in vision, hearing, and somesthesis. In one case, that of the dog, three auditory areas have turned up. The eventual study of these areas and their function in learning ought to take us a long step forward in understanding what goes on in the brain in conditioning and learning.

Allen has made a stab at this problem by taking out different auditory and somesthetic areas and seeing the effects of such removal on simple and differential conditioned responses (in the dog). His conditions of experimenting are rather complicated, and so are his results. Moreover, they are based on very few animals and they do not always fit in with the other facts described in this chapter. For those reasons we have omitted any detailed description of his experiments. The interested reader, however, will find the references in the bibliography and can look up the original papers.

THE NEURAL LOCUS OF CONDITIONING

So far in this chapter we have considered spinal conditioning, decorticate conditioning, and conditioning and retention after removal of restricted areas of the cerebral cortex. Now, in this last section, we can look at the problem somewhat more generally. We may ask such questions as, What routes are set up in the nervous system when learning takes place? What centers are of special importance in learning? Or, in a word, where in the nervous system can we look for the locus of learning?

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[1] Raab and Ades, p. 83.

There are a considerable number of studies pointed at these problems. They employ many different techniques, such as electrically stimulating the nervous system, freezing or temporarily paralyzing nerves and areas of the brain, and using different drugs to block or depress certain nervous functions. All these experiments, regardless of the physiological technique, however, have used some type of conditioning, either classic or instrumental. The various experiments can be arranged according to the aspect of the problem that they attack.

What Route? One particular question we can ask is whether conditioning takes place in the pathways of the unconditioned stimulus, in those of the conditioning stimulus, or at some other place in the nervous system. Kellogg has some interesting observations on this point. They do not rest on any surgical disturbance of the nervous system but come from experiments with the effect of sleep and drugs on conditioned responses. For example, in the typical buzz-shock experiment—dogs giving paw-flexure responses to avoid shock when a buzzer is sounded—dogs appear to doze off to sleep for brief intervals. When they do, their conditioned responses disappear but their unconditioned responses to shock do not. Similarly, if the dogs are given a light dose of some soporific drug like nembutal, they may lose their conditioned responses but not their shock-escape, unconditioned responses. Kellogg interprets both these facts to mean that there must be different neural centers involved in the conditioned and unconditioned responses.

Is the Unconditioned Response Necessary? Other experiments attack more directly different parts of the unconditioned and conditioned-response pathways. Several, for example, concern the question of whether it is necessary for the unconditioned response to occur in order for learning to take place. In one set of experiments the muscles involved in the conditioning response were paralyzed during conditioning by crushing the motor nerves leading to them (Kellogg *et al.*, Light and Gantt). A complete conditioning procedure was carried out while the dog could not respond. Then time was allowed for the nerves to regenerate, and when it was clear that the muscles could respond again, the animals were tested for conditioning. They showed by the appropriate flexure of the paw to the conditioning stimulus that learning had taken place while the muscles were paralyzed. These experiments are subject to criticism, because the paralysis did not prevent the animals from giving generalized struggle responses centering about the limb during the original conditioning. These generalized responses were conditioned, and it is possible that it was through them that the correct response was made after nerve regeneration.

Other experiments giving similar results, however, are not subject to this question. In one of them, morphine was employed as the unconditioned stimulus for evoking salivation in the typical Pavlovian type of conditioning (Crisler). The salivation, however, was blocked by giving the animal atropine during the conditioning trials. Testing later, without the atropine, produced conditioned responses of salivation to the conditioning stimulus. In a similar study, acid was used as the unconditioned stimulus for salivation, but salivation was again prevented with atropine (Finch). When conditioning tests were made later without atropine, the animal showed conditioned responses. These experiments blocking the motor response artificially thus show clearly that response need not occur in order for learning to take place. The parts necessary for learning, therefore, lie upstream from the muscles or glands involved in the learning.

Taking a step backward to the motor routes of the spinal cord, we find that these are not the locus for learning either. Loucks and Gantt, instead of evoking paw flexure by the conventional shock to the foot, did it by stimulating the motor roots of the spinal cord directly with an electric current. There was no sign of learning with this technique.

Are Motor Centers the Locus of Learning? Pushing even farther back into the nervous system, we come to the motor areas of the cerebral cortex, which are rather essential in carrying out any voluntary or learned response. In higher mammals, extirpation of the motor cortex causes serious paralysis. By stimulating the motor cortex electrically, we can evoke the various kinds of movements that occur in conditioned responses. By pairing such electrical stimuli with a normal conditioning stimulus, one can carry out a conditioning experiment. In one experiment, after the usual appropriate number of conditioning trials, tests were made of whether conditioning had taken place (Loucks). None had.

A second experiment, rather than employing stimulation of the motor cortex, used a technique for paralyzing it (Harlow and Bromer). During the usual conditioning trials, a large area of the cortex of the monkey was 'frozen' by the use of a special drug. This drug prevented responses of the limb to the unconditioned shock stimulus, and there was a complete flaccid paralysis. After the drug used for freezing wore off, however, conditioned responses were observed. These were not movements of the limb, but responses of the eyelids and head and neck, which naturally appear in response to shock. These responses now occurred when the conditioned stimulus, a bell, was sounded. Thus it was clear that learning had occurred, although the complete motor system from the cerebral cortex on down was paralyzed.

Unconditioned Stimulus. From these various experiments on motor systems and pathways, we can form the definite conclusion that the locus of conditioning is someplace other than the motor pathway of the nervous system. To see what the other places may be, we may turn to other studies that attack the role of sensory centers and pathways in learning. These give us some hints, although, unfortunately, they do not give us the final conclusion. The main idea of all the experiments is the use of direct electrical excitation of some part of the nervous system in place of either the unconditioned or the conditioning stimulus. By seeing whether such substitutions could be successfully made at various points, it was intended to get some idea of the centers and routes of importance for conditioning.

Sensory Pathways. Several studies show that stimulation in any part of the sensory system of the unconditioned stimulus up to and including the cortex will suffice for conditioning. When Loucks and Gantt were stimulating the spinal roots, in place of using shock-evoked leg flexion, they noticed that when the intensity of the stimulation was great enough to spread over into the sensory pathways, they were able to get conditioning to the buzzer. This they interpreted as the electrical stimulus serving as a substitute for foot shock in activating the pain pathways leading upward to the brain.

Cerebellum. In another study by Brogden and Gantt there is a very interesting result. Direct electrical stimulation of the *cerebellum* of the dog was substituted for the usual unconditioned shock to the foot pad. As usual, a sound was the conditioning stimulus. The cerebellar stimulation evoked movements of the same sort as those evoked from the motor cortex. Strangely enough, after a normal number of conditioning trials, pairing buzzer and cerebellar stimulation, a conditioned flexion of the limb to buzzer appeared. That is extremely interesting, but we cannot be sure what it means. The investigators assure us that the cerebellar stimulation was not spreading to the cerebral cortex, and we can rule out that possibility. Recent anatomical work, however, makes it clear that there is sensory representation of cutaneous senses in the cerebellum, and it is possible that the effect was through sensory pathways (Dow and Anderson, Snider and Stowell). Thus we do not know whether this phenomenon is to be regarded as a substitution of the sensory counterparts of the unconditioned stimulus or whether it is to be regarded as a more or less direct arousal of the unconditioned response.

Conditioned Stimulus. In all the studies in which an electrical stimulus to the nervous system is substituted for a conditioning stimulus we find affirmative results. Even such stimulation of the motor cortex results in conditioning. In Loucks's study, eliciting a hind-leg movement of the dog by cortical stimulation could serve as the conditioned stimulus for a reaction of the forelimb, when shock was the unconditioned stimulus. Anatomists tell us that there is representation of cutaneous sense in the motor cortex (Bucy), and we might assume that the result is due to cortical sensory stimulation. That assumption is borne out by controls run by Loucks in which he completely narcotized the hind limb during the conditioning series so that no movement could occur. Conditioning still took place. In view, therefore, of other results with direct motor stimulation, it is plain that in this experiment the sensory effects produced by the stimulation were serving as the conditioning stimulus.

In another part of the same study, Loucks sounded a buzzer, then produced a forced movement of the hind limb by electrically stimulating the cortex, and rewarded the lift of the hind limb with food. Under these circumstances, conditioning occurred. The conditioning extinguished, however, when he no longer presented food. Thus it was clear that the conditioning was based on buzzer and food rather than upon cortical stimulation.

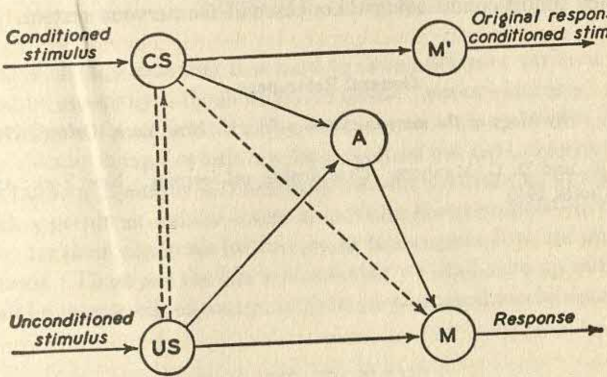

FIG. 150. Schematic diagram of the possible relations of areas and pathways involved in conditioning. There are four possible points of convergence of pathways in conditioning at which neural changes representing conditioning might occur: *CS*, the center excited by the conditioned stimulus; *US*, the center excited by the unconditioned stimulus; *A*, some association center or pathway; and *M*, the motor center for the unconditioned response. (*From E. Hilgard and D. Marquis. Conditioning and learning. New York: Appleton-Century-Crofts,* 1940. *P.* 319. *By permission of the publishers.*)

Finally, let us note another fact which is very much to be expected (Loucks). Direct electrical stimulation of the visual area of the cerebral cortex can serve as the conditioning stimulus. This was tried and proved true in two different conditioning situations, the salivary response to food and the flexor response to shock. It simply means that one can substitute direct excitation of the visual cortex for the use of a light.

Conclusions. That is where this particular story ends, although it is by no means a satisfactory ending. All it tells us is that the locus of conditioning is someplace in front of the final common motor path from the cortex (see Fig. 150). We do not know whether the neural changes that occur in learning are in the centers for the unconditioned stimulus, those for the conditioning stimulus, some third 'association' center, or some combination of all three.

Back in 1938, hope appeared for a brief moment that learning might be found in special association centers. Culler reported that a spot on the anterior ectosylvian gyrus, not normally concerned in bell-shock conditioning, would evoke the conditioning response if it were stimulated electrically after conditioning trials. It now appears that this was an artifact of changing sensitivity of the cortex through repeated stimulation (*cf.* Tower). At any rate, there have been no further claims for this association center either by Culler or by others. So we are still in the dark.

Obviously, there is much to do in the future with either the kinds of techniques already used or new ones to be developed, to locate the areas and pathways in which simple conditioning takes place in the nervous system.

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CHAPTER XXII

SENSORY LEARNING

We have already said that it is hard to define different varieties of learning. It would be especially difficult to try to define "sensory learning" so that it is clearly different from "conditioning," which we took up in the last chapter, and "problem-solving," which we shall meet in the next chapter. The term *sensory learning* is simply a convenient one, for it covers all kinds of learning in which a person or animal learns something about stimuli—to discriminate them, to use them as signals for choices, or to recognize their meaning for satisfying needs. These are the kinds of learning we shall take up in this chapter. We shall be interested, of course, in their physiological mechanisms.

SOME PROBLEMS

Before we get into the fine points of the matter, we ought to think briefly about some of the problems we face in studying the physiological mechanisms of sensory learning. Special problems and barriers to progress have probably been more numerous in this area than in most areas of physiological psychology. It is important to understand what these problems are in order to appreciate both the value and the shortcomings of the experimental facts. It is also important to realize that we may expect very rapid strides in the near future because new and potent techniques, which we shall describe in a moment, have recently been devised.

BEHAVIORAL METHODS

In trying to get at the neural mechanisms of sensory learning, our main tools are extirpation and training. We train an animal to master a particular discrimination, we then try to see whether the animal is capable of remembering the discrimination or, if not, of learning it again after we have removed a particular part of the brain. In principle, using these tools is straightforward. In practice, however, there are some hitches.

Sensory Capacity. In the first place we must distinguish between sensory capacity and learning capacity. It is theoretically possible for an animal's senses to be perfectly all right and yet for it to be unable to learn a particular problem. Conversely, it is possible for a person or animal to be able to learn a discrimination and yet to fail because the sense upon which he must depend for cues may be impaired. When, however, we are using some method of training as our tool in research, we cannot always tell whether failures we may get are due to losses of learning ability or of sensory capacity. If, for example, an operated animal fails after long training to discriminate between a triangle and a circle, we may not be sure whether the difficulty is that he cannot "see" the stimuli or that, seeing them, he cannot learn their meaning. Sometimes we are able to settle such a question as this by devising other methods of measuring sensory capacity. There are times, however, when it seems impossible to find a way of separating sensory capacity and learning ability. This is one of our difficulties in studying the mechanisms of sensory learning.

Learning Methods. We should realize, too, that our methods of measuring learning have several faults. (1) They are not always too reliable. Animals may differ widely among themselves in their learning scores, and they may be rather inconsistent in their performance from trial to trial. (2) We are not always sure that we are measuring the significant aspects of learning. Animals frequently must learn three or four things to reach the criterion of discrimination that we hold up. Yet our measures, such as the number of correct and incorrect responses, may not be fair measures of, say, any but the final stage of learning. If it happens in such a case that our brain operation affects an earlier stage than the one we are measuring, or a different aspect of learning, we will completely miss the fact in our records.

Other Factors. In addition, there are a lot of annoying details of method that may get in our way when we try to study sensory learning or any complex type of learning. One factor, which can make a big difference, is whether or not we punish an animal for errors as well as reward it for successes (Krechevsky). Another is the kind of apparatus we use. For example, research workers failed for years to get rats to discriminate visual patterns. They succeeded only when they hit on a particular type of apparatus that was necessary to make the rat look at the patterns (Fields, Munn, Lashley). A third factor is what stimuli are rewarded and punished. Animals sometimes learn much better with one stimulus than with another.

With no trouble at all we could add many more factors to this list. There is no need, however, to go into all the details. The main point to bear in mind is that our behavioral methods have their weaknesses. These weaknesses sometimes leave us up in the air about the conclusions to draw from our research. Sometimes they even lead us to the wrong conclusions.

AREAS OF THE CORTEX

Our behavioral methods are not our only difficulties. There are also troubles on the side of anatomy and physiology. Some of them we did not know about until recent research brought them to light, but now that we do know about them, our future research can be much more profitable.

Anatomical Areas. As we explained in earlier chapters (see pages 48, 208, and 267) different regions of the cerebral cortex have been classified in various ways. Until recently our main classifications were based on anatomical methods. Brodmann's system, which we have used a lot in this book, was based on differences from region to region in the structure of the cortex. Later anatomists looked at Brodmann's areas to see what fibers projected upward to, and downward from, these cortical areas. By purely anatomical methods they tried to figure out what areas of the cortex might be primarily sensory in function and what areas seemed to be "association" areas, *i.e.*, areas concerned in learning and memory.

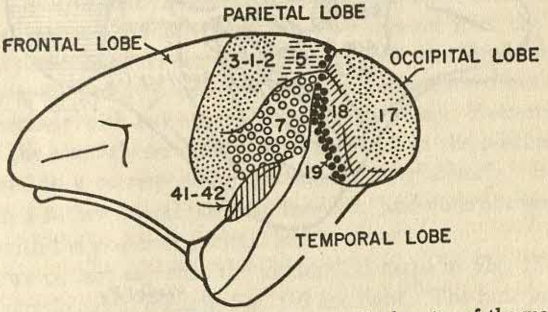

FIG. 151. Diagram of the anatomical areas of the cerebral cortex of the monkey supposed to be concerned in sensory functions. Area 3–1–2 (postcentral gyrus), primary somesthetic cortex; areas 5 and 7 (posterior parietal lobule), somesthetic "association" area; area 17 (striate area), primary visual area; areas 18 (peristriate) and 19 (parastriate), visual "association" areas; and area 41–42, the auditory area. This latter area is shown as though the lateral fissure, in which it is partly buried, were spread apart.

We have had many views of the cortex and its areas in the various chapters of this book. In Fig. 151 you see another view only slightly different from those you have seen before. This one shows what we have thought, on the basis of the classic anatomical methods, are the areas important in sensory, discriminative, and associative functions. In addition to area 17 (the striate area), two areas near by, numbered 18 and 19, have been regarded as visual association areas. In addition to the primary somesthetic cortex of the postcentral gyrus (area 3–1–2), a large part of the parietal lobe (areas 5 and 7) the posterior parietal lobule, has been thought to be a somesthetic association area. In higher animals there have been vague but rather uncertain attempts to identify an auditory "association" area. You can see it also depicted in Fig. 151.

Most of the experiments that have been done in the last thirty years have been based in some degree on the anatomical areas shown in Fig. 151. It was one or another of these areas that experimenters took out to see what would be the effects on discriminative learning or retention. Occasionally they did exploratory experiments, taking out many different areas, but such experiments were of little value because they did not correspond to the anatomical areas.

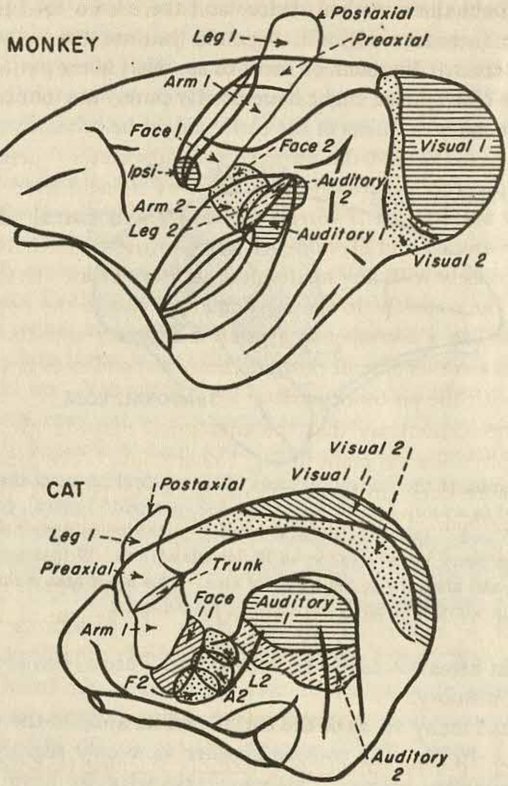

FIG. 152. Maps of the sensory areas of the cortex gotten by means of electrical recording from the cortex during peripheral stimulation. The lower left part of somatic face area I is for ipsilateral projection. In the diagram of the monkey, the lateral fissure is spread apart to show the auditory areas on its upper and lower banks. The postaxial part of somatic area I lies down in the longitudinal fissure but is "unrolled" in the diagrams for the cat and monkey. *F*, face; *A*, arm; *L*, leg. (*After C. N. Woolsey. Patterns of sensory representation in the cerebral cortex, p.* 438. *Fed. Proc.*, 1947, 6, 437–441.)

Physiological Areas. We have learned only recently that anatomical methods do not tell us the whole story. They sometimes do not reveal the existence of areas or of pathways that are in fact there. Sometimes they mislead us into placing special importance on a tract or area that is especially prominent. In many cases it appears that anatomical areas may mean very little in terms of the functions in which we are interested.

Physiological methods, at any rate, give us a rather different picture (see Woolsey). These are the methods of electrical recording during various kinds of stimulation and of local strychninization of various parts of the brain. We have talked about these methods before and there is no need to go into them in detail here (see page 35). In Fig. 152 you see the net result of these methods. There are diagrams of two brains: one for the cat and one for the monkey. The chimpanzee might have been included too, but in most respects it is like the monkey.

You see in Fig. 152 that the primary and "associative" areas of the cortex are distributed rather differently from what we thought from the anatomical maps. Visual areas I and II correspond rather well with Brodmann's 17 and 18. Auditory areas I and II, however, are two well-defined areas that do not correspond precisely with any anatomical auditory areas. Even more striking is the map of the somesthetic areas. Somatic I lies in the postcentral cortex in monkeys and in a corresponding position in lower animals. Somatic area II turns up in a rather lateral position, however, and does not seem to correspond at all with the posterior parietal lobule.

Of course, we cannot say that the anatomical maps in Fig. 151 are wrong and that the physiological maps in Fig. 152 are right. The functional method, however, is more likely to be significant from our point of view than is the anatomical method. Unfortunately, the physiological maps are so new and recent that there has not been time to make use of them in physiological experiments with sensory learning. Of the many experiments we shall discuss, therefore, practically all have been based on the anatomical maps. In time, however, we will have new experiments based on physiological maps.

SOMESTHETIC HABITS

There are three main categories of sensory learning that we shall take up: somesthetic, auditory, and visual learning. The order in which we consider them is somewhat arbitrary, but starting with somesthesis and ending with vision ought to be satisfactory.

Research workers have not yet looked into the physiological mechanisms of learning or remembering thermal or pain discriminations. They have, however, investigated kinesthetic habits (weight lifting) and such tactual habits as discriminating the roughness and the shape of objects. Rats, monkeys, and chimpanzees variously have been the subjects used in the researches.

Roughness Discrimination in the Rat. Already mentioned in an earlier chapter (Chap. XII) is one experiment with the rat concerning tactile discrimination and the cortical areas that are involved in it (Smith). Rats were run in a Y apparatus in which they found two different sandpapers, one rough and one smooth, at the fork of the Y. They were supposed to take the path of one of these sandpapers to get to food. This discrimination is comparable to a light-dark visual discrimination or an on-off sound discrimination.

Smith made various lesions, large and small, in various parts of the rat's cortex. Most of these lesions did little or nothing to the roughness discrimination habit. There were four rats, however, who showed complete amnesia for the habit, and in addition, three others whose performance was doubtful. On reconstructing diagrams of the rats' brains, Smith found that the area you see in Fig. 153 was common to all four animals with postoperative amnesia. The area lies in the dorsal and frontal part of the brain.

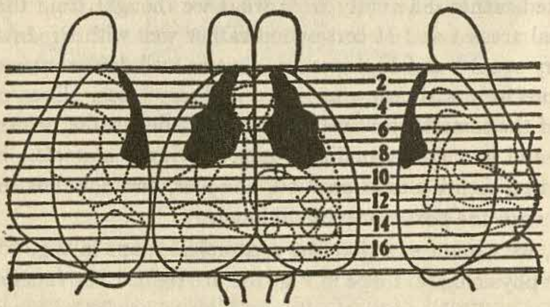

FIG. 153. The area bilaterally common to the lesions of four rats that suffered postoperative amnesia of the ability to make a tactile discrimination of the roughness of sandpaper. (*From D. E. Smith. Cerebral localization in somaesthetic discrimination in the rat, p.* 173. *J. comp. Psychol.*, 1939, 28, 161–188. *By permission of Williams & Wilkins, publishers.*)

Whether this area is the "association" area for somesthetic habits in the rat is very questionable. For one thing, there are logical objections to delimiting the area by taking what is common to several animals. Moreover, Smith had some rats with lesions running well into "the area" that showed no postoperative loss. In addition, the area is not very reasonable, for it runs far forward in the brain and includes a good deal of the "motor areas." Finally, the area in Fig. 153 does not correspond at all with the somesthetic areas that have been mapped in the rat's brain either by anatomical or by physiological methods (*cf.* Figs. 151 and 152). It looks, therefore, as though we must have more research before we know the truth about somesthetic "association" areas in the rat.

Tactual Discrimination in the Dog. In some work by Allen, we have one of the few attempts to find out what the somatic areas I and II do in cutaneous discrimination. The method he used was really a conditioning method, for he had dogs raise their paws when a tactual stimulus was applied. By having them also keep their paws on the ground when another kind of tactual stimulus was presented, he got them to discriminate two different stimuli. When he removed somatic area I, there was some loss in the discrimination, but not much, and it was clear that the dogs had some memory for it. When he took out somatic area II, however, the dogs had a complete amnesia for the habit and had to be retrained. The number of retraining trials necessary, moreover, far exceeded that in the original training. From these results, it looks as though somatic area I has little to do with learning or remembering a tactual discrimination but somatic area II is rather important in such a memory function.

Tactual Discrimination in Primates. We also have some experiments on roughness discrimination in the primates. Both monkeys and chimpanzees have been used, although not in any large numbers (Ruch). The lesions that have been made are based on anatomical methods of mapping the cortex rather than on the more recent evoked-potential methods. Thus the lesions have been made in area 3–1–2 (roughly, somatic area I) and in the posterior parietal lobules. Here in brief are some of the results and conclusions:

Taking out the posterior parietal lobe in either the monkey or the chimpanzee causes some loss of memory of the roughness discrimination habit. The loss is much greater in the chimpanzee than in the monkey. The postoperative amnesia, however, can be overcome by a moderate amount of training, more in the chimpanzee than in the monkey. Removing the entire parietal lobe, *i.e.*, both the postcentral gyrus and the posterior parietal lobule, causes an even more serious disruption of the habit. This operation, as we have already learned (see page 271), affects not only the habit but also the sensory capacity of primates to make somesthetic discriminations. It is no wonder, then, that it takes very prolonged retraining to get an animal to reestablish the roughness discrimination habit.

Kinesthetic Discrimination in Primates. In a moment we shall come to more complex types of tactual discrimination. The results for kinesthetic discrimination, however, are more comparable to those for roughness discrimination. It is therefore more logical to deal with them first. Monkeys were first trained to discriminate differences in weight, and the effect upon retention of the discriminative habit was measured after removal of the precentral, postcentral, and posterior parietal areas, taken separately and together.

After the separate removal of any one of these areas, there was some loss of memory for the discrimination, but after retraining, the discriminations could be mastered again. The memory loss was much slighter after removal of the precentral and postcentral areas than after destruction of the posterior parietal areas. With combined lesions of the precentral and postcentral areas there was still only a moderate loss of memory for the discrimination, and this was easily effaced by training. A combination of the postcentral and parietal "association areas," unfortunately, was not performed.

As matters stand, we might conclude that ability to learn and to retain kinesthetic discriminations in the monkey does not depend upon any particular restricted area of the cortex. This may be in error, however, for not all possible areas and combinations of areas have yet been tried. For one thing, we have not yet had tests either of discriminative capacity or of learning and retention when somatic areas I and II have been taken out.

Some of the same experiments on kinesthetic discrimination have been done with the chimpanzee that have been done with the monkey. The results in general are the same, except that the effects are somewhat worse in the chimpanzee than in the monkey. This result falls in line with what we might expect from the principle of corticalization in evolution.

Tactile Form Discrimination. Finally, let us consider the most complex type of somesthetic discrimination, the tactual discrimination of form. This is called *stereognosis*. This capacity is relatively easily destroyed. Removal of the posterior parietal lobule alone, for example, is sufficient to cause complete amnesia for stereognosis. In the case of complex form discriminations, no amount of retraining will yield mastery of the discrimination, although with less difficult discriminations retraining is effective. If subjected to long retraining, a chimpanzee whose posterior parietal lobule has been removed may learn again to distinguish between a cone and a pyramid, but the capacity to discriminate a pyramid and a wedge, which are much more alike than a cone and a pyramid, is never regained no matter how many trials are given the subject.

This finding indicates (1) that stereognostic learning depends upon the posterior 'parietal association' area when it occurs in the normal animal; and (2) that after removal of the area some other structure takes over part, but not all, of the learning function. We do not know whether this other structure is subcortically or cortically located. It is possible, for example, that the postcentral gyrus mediates the relearning of simpler stereognostic discriminations after removal of the posterior parietal area. So far, however, we have no experiments to check this point. Nor do we know about the alternative possibility that subcortical centers may perform the function.

AUDITORY DISCRIMINATION

We are not especially proud of what we know about the brain mechanisms for auditory habits. In the first place, there are not as many experiments as we might hope for. In the second place, both the behavioral methods and the anatomical controls that have been used are rather crude. And in the third place, there is some disagreement among the results. Nevertheless we shall summarize briefly the principal results and interpretations.

Intensity Discrimination. There are a variety of techniques for training animals to distinguish the presence or absence of a sound or the difference between sounds of different intensity. Most of the research concerning brain mechanisms has used a simple presence-or-absence method. The rat, for example, can be made to shuttle from one end of a grill to another (Eccher) or to hop on or off a platform (Hunter and Pennington) when a sound is turned on. In the dog, the most common method has been to have the animal lift its foreleg when a sound comes on—on threat of shock. In the cat, a common method has been to put the animal in a running cage and punish the animal if it does not run when a sound is made.

Learning. There is unanimous agreement on one point, that animals can learn these habits perfectly well without their auditory cortices. Most of the experiments at hand were done before we knew about the existence and location of auditory areas I and II, so it has not always been clear just what is meant by the auditory area. No matter how large the lesions made, however, or where they have been made, animals have always been able to learn a simple reaction to a sound going on or off.

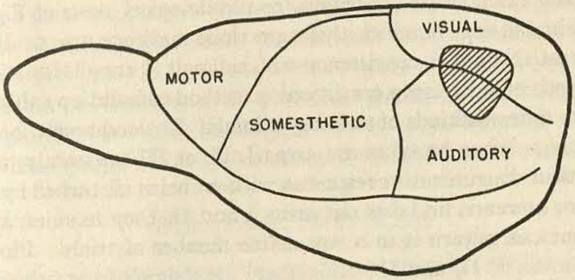

FIG. 154. Diagrammatic side view of the left cortex of the rat. The areas are those found by electrical methods of mapping the cortex. The crosshatched area is approximately the area Pennington found to be common to all the rats that had amnesia for an auditory habit after cortical lesions.

Amnesia. There is also rather general agreement concerning amnesia from removal of the auditory areas; *i.e.*, when an animal has learned a simple habit of responding to the onset of sound, it loses this habit when the auditory cortices on both sides are removed. In the rat, removal of auditory areas always has serious effect on the habit and the animals need more training to reacquire it (Wiley, Pennington). We cannot be sure whether, in such cases, the animals completely forget the habit and have to relearn completely. The data are simply hard to interpret in this regard. In the dog and cat, however, we can be more sure of such a conclusion (Raab and Ades). Removal of the auditory areas causes amnesia—apparently quite complete amnesia—but the animals are capable of relearning the habit.

Locating Auditory Areas. Investigators have made attempts to find the location of the auditory cortex by measuring the effects of various cortical lesions on auditory memory. Their practice has been to operate on large numbers of animals and then to find the area common to those animals which showed some disruption of the auditory habit. In going about the problem in this way, they have assumed that the entire auditory "association" cortex must be destroyed before the auditory habit is disrupted and also that lesions outside the auditory cortex have no bearing on the habit. Actually, both assumptions are open to question, and consequently so are the conclusions of their work.

We have, nevertheless, maps of the area of the rat that seems to be necessary for memory for simple auditory habits. In Fig. 154 you see the map of Pennington's "subordinate area." This is a rather small area, regarded as part of the auditory area, that he found when he used pure tones and got the area common to all rats with postoperative amnesia.

Auditory Areas I, II, and III. Unlike these studies we have just summarized, Allen has done one based on the physiological areas of Fig. 152. He has used it in the dog, in which there are three auditory areas. He calls the third one area C, but for consistency we shall call it area III. Moreover, as in somatic problems, he uses a conditioning method to build up a discrimination between two different kinds of auditory stimuli. The end result, however, is a discrimination. When he takes out areas I, II, or III separately, the dogs go on making their discriminative responses without being disturbed by the operation. When, however, he takes out areas I and II, they have an amnesia for the habit but can relearn it in a reasonable number of trials. Finally, when he removes areas I, II, and III altogether, the animals forget the discrimination and can never relearn it after more than 1,000 trials. It is too early to say exactly what these results mean. This kind of research, however, may eventually lead us to some sensible conclusions about the role of the auditory areas in learning.

Localization. Several experiments with both the rat (Wiley) and the cat (Neff and Yela) concern auditory localization. Boxes have been so arranged in such experiments that the animal approaches an intersection and hears a sound coming from a box located at the end of one of two or more paths. The animal must choose the correct box to get rewarded. Thus he makes a localization of a noise or tone in space.

Now when this method has been used in rats, the results are no different from what they are for simple intensitive habits. When the auditory areas are removed, animals that have formed the habit previously are no longer able to do it and thus suffer amnesia. They are, however, able to relearn the habit in normal time. Recent experiments with cats, however, present us with more complicated results (Rosner and Neff). In the first of several experiments, the investigators used as sources of sounds three boxes that were not very widely separated (in angular distance). Under these circumstances, cats subjected to ablation of auditory cortex lost the localization habits set up preoperatively and were not able to relearn them. Changing the problem, however, so that the animals had to localize sound in only one of two boxes, separated by about 180 deg., gave a different result much more like that of the experiments with rats. After operation, the cats forgot entirely, or almost entirely, their preoperative habits, but they were able to relearn them again.

VISUAL INTENSITY

As you might imagine, by far the greatest amount of research on sensory learning has been done with visual discriminations. Visual stimuli are rather easy for experimenters to make up and to use in experiments. Then too, the visual system of the brain is well known, and it is relatively accessible to experimental surgery. For these reasons, and perhaps others, we have acquired more information about visual learning than about all other types of sensory learning put together.

To make a somewhat better outline, we have divided visual learning into its main aspects: intensity, movement, pattern, and color. There will be a section on each of these topics. In each case we shall consider what is known at present about the brain mechanisms of the particular aspect of visual learning. This section starts off with visual intensity, which we know from our previous discussion of vision (pages 146 to 171) is the most primitive of the visual capacities.

Subcortical Mechanisms

Just to make the story complete, we should mention studies of how subcortical centers, particularly the thalamus and superior colliculi, function in the learning and retention of an intensity discrimination. The stereotaxic technique lets investigators make lesions electrically in the deep parts of the brain without much damage to the cortex. Ghiselli and Brown have used this technique in studying a number of learning functions, and we shall see what they found in subsequent sections of this chapter and the next. All their work has been done with the rat.

Thalamic Nuclei. As you might expect, they found no effects of injuring the anterior thalamic nuclei or the corpus striatum. The latter is primarily a motor center—part of the extrapyramidal system—and the former, we know, ties in closely with the mechanisms of emotion (see page 352). On the other hand, damage to almost any of the other thalamic nuclei seems to decrease the rate of learning an intensity discrimination—even though the cortical areas to which these parts of the thalamus project have nothing to do with visual learning (see below). More than that, the *mass* of the thalamic nuclei destroyed is proportional to the amount by which learning is retarded. This is a phenomenon that we ordinarily see only in maze learning (Chap. XXIII). At present there is no certain interpretation of it.

Superior Colliculi. One study (Ghiselli) has also looked into the function of the superior colliculus. This, we know, is the main subcortical center for vision. It tells us two facts that are worthy of note. One is that bilateral removal of the superior colliculi by themselves does nothing to the memory of, or the ability to learn, a visual discrimination based on intensity. The second is that removal of the colliculi after the visual cortex has also been removed (see below) causes amnesia for the discrimination. Animals, however, could relearn the discrimination after due training. If we take these facts at their face value, they mean (1) that the superior colliculus is normally not involved in intensity discrimination, (2) that in the absence of the visual cortex the colliculi mediate such a discrimination, and (3) that neither the cortex nor the colliculus, but rather some other center, is absolutely necessary for the learning of a visual intensity discrimination.

VISUAL CORTEX

Probably the best established fact in the general area of sensory learning is that removal of the visual cortex causes an animal to lose the habit of intensity discrimination. This experiment has now been done a number of times in the rat, cat, and monkey. These animals may be trained to choose the lighter or darker of two panels and then, upon surgical removal of their striate areas, will lose all their training and act as though they never saw the problem before. An equally well-established fact is that animals without a visual cortex can relearn an intensity discrimination. Although they forget what they learned preoperatively, they are perfectly capable of learning the intensity discrimination again.

Postoperative Learning. There are some questions about the rate of postoperative relearning. Under some circumstances the rate is just the same as before operation. That is when the discrimination is a light-dark one and when punishment is used for incorrect responses as well as reward for correct responses (Lashley). Under other conditions, however, postoperative learning may be decidedly inferior to normal learning.

Differential Discrimination. One of these other conditions is learning a differential discrimination, that is, to distinguish a light panel from one that is not quite so light. In this discrimination rats without their striate cortices are retarded. Such a differential discrimination, of course, is more difficult to learn than a simple light-dark discrimination. We should bear in mind, too, that animals without their visual cortex are not able to discriminate differences in intensity as well as normal animals (see page 169). Indeed, this loss in sensory capacity may well explain the inferiority of the operated animal under these conditions.

Lack of Punishment. One other training condition yields inferior postoperative performance. That is training without any punishment for errors and only reward for correct responses (Krechevsky). In this case animals require more errors and trials postoperatively to learn an intensity discrimination than they do preoperatively. Why this is true we do not know, but it is rather common to find that there is less motivation, or that greater incentives are required, after cortical lesions than is normally the case (see page 503).

The Problem of Amnesia. The loss of memory without loss of capacity to relearn the intensity discrimination following lesion of the visual cortex is one of the major mysteries of cortical function. It is somewhat like the general phenomenon of recovery of function that we meet with often in brain functions. In one way or another, when one of its mechanisms is damaged, the brain seems to supply some alternate mechanism for looking after its business. In this case the striate cortex is part of the normal mechanism, but in its absence some other center in the thalamus or midbrain takes over the task of learning the intensity discrimination.

Why and how one center of the brain can take over the functions of another center is the mystery. Research on this problem will probably go on for some years to come. At present there are three main possibilities (*cf.* Lashley). One is that striate lesions so change the visual capacity of the animal that it must thereafter use completely different aspects of the discrimination situation to solve the problem. We know, of course, that striate animals lose their detail vision and thus lose their ability to perceive spatial aspects of stimuli (Lashley, Klüver). Perhaps this, in some way or other, explains the amnesia.

Lashley tried to test this hypothesis some time ago by destroying the lens in rats' eyes, thus destroying their detail vision, before original learning. In this way he hoped to make animals "see" the discrimination problem in the same way before cortical operation and afterward. When operated on, however, these animals showed the same loss of memory with ability to relearn as did all the other experimental animals we have been talking about. This experiment, therefore, seems to rule out the first possibility.

The two other possibilities are still to be tested. One is that postoperative changes in discriminative capacity cause the amnesia. We know that animals without the striate cortex cannot discriminate visual intensity as well as normal animals (see page 169). Perhaps this fact in some way explains the amnesia. The final possibility is somewhat vague, but it is that some "reorganization" of functions follows removal of the visual cortex. Perhaps the visual cortex normally holds certain other centers under restraint, and these centers are free to function in the absence of the visual cortex. Certainly this kind of thing happens in the nervous system, as we have seen in the cases of both emotional behavior and motor functions.

Amount of Visual Cortex. Knowing that removal of the *entire* visual cortex causes a complete amnesia for the intensity discrimination habit, we may ask next what happens when only part of the visual cortex is removed. Is there partial amnesia, or can a small part of the striate cortex "retain the whole memory"? Experimental results on this question have been difficult to interpret, and we have had first one answer (Lashley, 1929) and then another (Lashley, 1935). The final answer seems to be that rats have just about perfect memory for the discrimination if a relatively small part of the striate cortex is left intact. We may conclude, therefore, that memory can be "stored" in a small portion of the striate area.

Conditioning and Discrimination. As a last comment about the striate cortex and intensity discrimination we have one more mystery to note. When we remove the striate cortex from animals that have been trained to *discriminate* differences in intensity, they lose the habit and must learn it all over again. That is what we have just been talking about. If, however, we remove the striate cortex from animals that have been *conditioned* to respond to differences in intensity, say, by raising their legs, there is no loss of the habit and no necessity for retraining. That fact was discussed at length in the last chapter (page 452). The mystery is why there is a difference between conditioning and discrimination. When that mystery is solved, we probably will have a better idea why striate lesions cause amnesia for the discriminative habit.

OTHER AREAS OF THE CORTEX

There has been some research, but not a great deal, on other areas of the cortex and the role they play in learning and remembering an intensity discrimination. Both the methods and the results of such research fall into two separate categories.

Simple Discrimination. One method is the one we have been talking about throughout this section. An animal is faced with two panels, one lighter than the other, and chooses one of them. If correct it gets food and if incorrect it is punished. When this method is used, no part of the cortex other than the striate cortex seems to have anything to do with either the learning or retention of the discrimination. At least, lesions at different places in the rat's cortex have no effect on learning or retention unless they involve the striate area (Lashley).

Maze Discrimination. Another method, however, gives different results. In this method an animal makes a series of choices as in a maze. At each choice point it faces two alleys, one lighter than the other. If it chooses correctly it goes on to another choice point, and after the last choice it gets food. If it chooses incorrectly it runs into a blind alley and must retrace its steps to the choice point. Visual intensity is the cue for running the maze correctly. Areas of the cortex other than the striate area seem to be important in this task. In fact, lesions almost anywhere in the cortex will do some harm to learning or retention, and the larger the lesion the greater the impairment (Krechevsky). This correlation between mass and performance has been called "mass action," and we shall deal with it at some length in the next chapter.

COLOR AND MOVEMENT

There is no point in wasting much time or space on these topics. They certainly are types of discrimination that are an important part of visual habits of man and the higher animals. The trouble is, however, that we know practically nothing about the central neural mechanisms either of the sensory capacities or of the learning of these discriminations. There are a few comments to make about color discrimination, but we can say them better later when we talk about form discrimination. As for movement discrimination, about all we know is that amnesia for movement discrimination follows removal of the striate cortex—just as in the case of intensity discrimination—and that relearning of the discrimination is possible, but only after very protracted training (Kennedy, Morgan). Beyond that fact we have few details, and it is pointless to try to make any more sweeping conclusions at this time.

VISUAL FORM DISCRIMINATION

Ability to learn and to remember discriminations among visual forms has had a great deal of attention from investigators. They have also tried hard to get at the physiological mechanisms of this type of sensory learning. They have been successful enough to let us draw some rather interesting conclusions.

Before we delve into them, let us get our terms straight. There are several terms that have been used with somewhat similar meanings: form, pattern, shape, and detail. All these terms refer to the spatial aspects of vision as contrasted with intensity vision. There are somewhat subtle distinctions between the terms, but they need not concern us here. We are going to use them interchangeably.

SUBCORTICAL FUNCTIONS

The visual system, we know, has a spatial projection from the retina to the visual cortex. We also know that the visual cortex is necessary for the capacity to see form and detail. We should expect, then, that injury anywhere along the line of the visual projection to the cortex might impair learning and memory for form discriminations. That is what experimental results show, for partial cutting of the optic nerves or injury to part of the lateral geniculate body slows down learning or impairs memory for such discriminations (Brown and Ghiselli).

Superior Colliculi. These are the end of the line of the subcortical visual pathways. Yet what they do in vision is not clear. We have just seen above that they are not necessary for learning an intensity discrimination. It turns out that they are not necessary for form discrimination either. In about the only experiment we have on this point (rats), removing the superior colliculi did not impair the rate of learning a form discrimination (Ghiselli).

Pretectal Nuclei. Interestingly enough, some nuclei that lie just in front of the colliculi, called the *pretectal nuclei*, are of some importance in learning form discriminations. These nuclei have always been thought of as reflex centers that receive impulses from the visual pathways and send impulses down to the ocular motor centers. In experiments by Brown and Ghiselli, however, rats with injuries in the pretectal nuclei took much more than the usual number of trials to learn a form discrimination. So they seem to have something to do with such learning. Perhaps they are important in turning and focusing the eyes or more generally in visual "attention." We do not know.

Thalamic Nuclei. As in the case of learning an intensity discrimination, other thalamic nuclei—*i.e.*, all except the anterior group—seem to be important in learning form discrimination. Animals with lesions in these nuclei take about twice as many errors to learn a discrimination as do normal animals. They are not, however, so important as the pretectal nuclei. What this fact means we do not now know.

CORTICAL FUNCTIONS

Back in the chapter on spatial vision (Chap. VII), we saw that the visual area of the cortex—otherwise known as striate area, area 17, or visual area I—is essential for the basic capacity to see visual form or patterns. Obviously, then, animals lacking the striate cortex cannot be expected to learn or remember a form discrimination—because they cannot see, not necessarily because there is anything wrong with their learning abilities. Quite aside from this point, however, there are a number of interesting and important questions about the function of the cortex in pattern discriminations.

The Striate Areas. One question is how habits of form discrimination fare when only part of the striate cortex is damaged. This cortex, we know, is arranged topically, *i.e.*, each point on the cortex represents some point in the visual field. Injury to part of the cortex, then, is like destroying detail vision in part of the visual field. This, of course, is a change in sensory capacity in part of the field. It is interesting to see how such a change affects learning.

Several studies make it clear that animals can both learn and retain habits of form discrimination when only part of their striate cortex is removed (Lashley, Settlage). Indeed, in the rat, an extremely small remnant of this cortex can serve to maintain a pattern discrimination (Lashley). On the other hand, when any fairly large portion of it is taken out, there is usually some disturbance of discriminative habits. Animals may act for a while as though they have forgotten discriminations that they learned before operations.

Such disturbances, however, are mostly a matter of sensory loss rather than of learning or memory. Two different experiments with monkeys make that rather clear. In one of them, seven monkeys had their occipital cortices removed on one side (Settlage). This produced 'cortical blindness' for about half the visual field. There was a temporary loss, but no final loss, in visual discrimination habits. The trouble seemed to be that the monkeys at first retained their preoperative habits of visual fixation of objects, and with large gaps in their visual field, they were sometimes unable to see the objects. As time went on, however, the animals gradually improved in ability to make visual discrimination, presumably because they were learning new habits of visual fixation and 'filling in' their visual field.

To test this hypothesis, another investigator carried out another experiment (Harlow). He kept some of these monkeys, which had their striate cortex out on one side, in the dark for a period of 10 days following the operation. Then he compared their ability in pattern discrimination tests with those of animals allowed in the light during this time. When brought out of the dark, the monkeys showed no recovery of ability to do pattern discrimination tests.

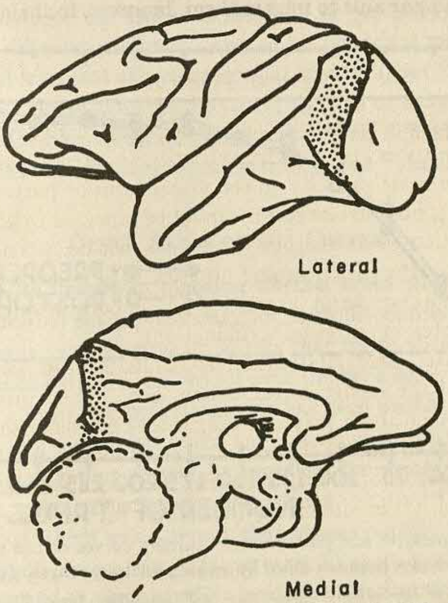

FIG. 155. A sketch of the medial and lateral aspects of the brain of the monkey showing the prestriate areas that Ades removed in his study of learning and memory of visual discriminations. The dotted area is the prestriate area (Brodmann's 18 and 19). (*From H. W. Ades. Effect of extirpation of parastriate cortex on learned visual discriminations in monkeys, p.* 62. *J. Neuropath. exp. Neurol.*, 1946, 5, 60–65. *By permission of the publishers.*)

If left in a lighted cage, however, for a few days with the opportunity to get new experience with visual fixations, the animals could regain the ability to do the discriminations of detail.

Prestriate Areas. There are two other areas that are regarded as part of the visual system of the cortex. One is the peristriate area, area 18, that lies next to the striate area. The other is the parastriate area, area 19, that has varying positions in different animals but looks as though it is more a part of the parietal lobe than of the occipital lobe. Area 19, you may remember, is the area that will arouse eye movements when stimulated by an electrical current. It is also a suppressor area, as judged by the strychninization technique (see page 295). Together these two areas may be called the *prestriate* areas (see Fig. 155)—they lie in front of the primary visual cortex (see Lashley).

Amnesia. Unfortunately, we have only two studies of the prestriate areas—both in monkeys—and these directly conflict with each other. One is by Ades, the other by Lashley. Ades had his animals learn three different discriminations, one of color, another of size, and a third of form. After they mastered the discriminations he took out the prestriate areas. After an appropriate rest he tested the monkeys, only to find that they had complete amnesia for all the habits. He was able to retrain them, however, to their original performance in about the same number of trials. In other words, Ades found the same kind of amnesia for form discrimination in the monkey after prestriate ablation that many investigators have found for intensity discrimination in several animals after striate ablation. Ades curves, as you can see in Fig. 156, are very convincing.

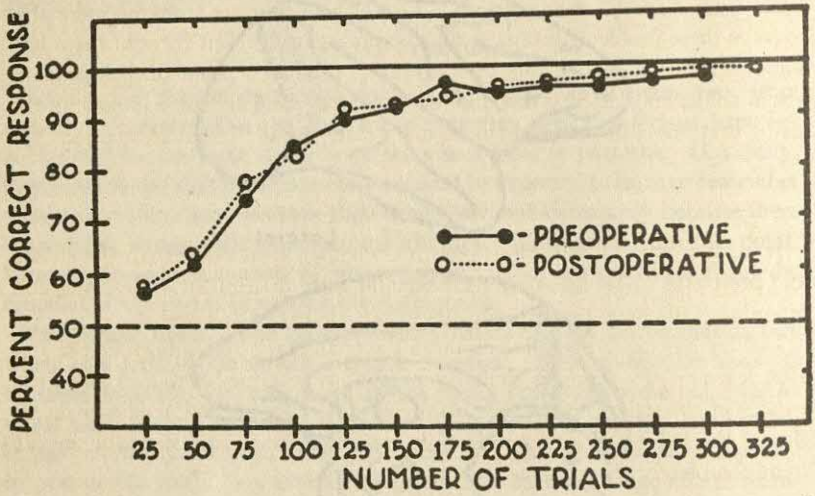

FIG. 156. The preoperative and postoperative learning curves of one of Ades' 'prestriate' monkeys. The curves have been smoothed by making rolling averages of threes. They represent size and shape discriminations combined. There appears to be complete amnesia after the operation but relearning at the normal rate. (*From H. W. Ades. Effect of extirpation of parastriate cortex on learned visual discriminations in monkeys, p.* 64. *J. Neuropath. exp. Neurol.*, 1946, 5, 60–65. *By permission of the publishers.*)

No Amnesia. Lashley has done practically the same experiments as Ades. In addition, he carefully checked and reported the location and extent of his brain operations, and he criticizes Ades for not doing the same thing. He, however, found no postoperative amnesia except in one case, which had some impairment apparently due to damage to the striate areas.

In four out of five cases, in fact, Lashley's lesions invaded the primary visual field, whereas Ades feels that none of his three monkeys had any such impairment. It is hard to tell how much each investigator got of the prestriate areas, but it looks as though Ades got more than Lashley did. We must have considerably more research along this line before we can come to any final conclusion.

Deserving brief mention here is one other test that Lashley ran on his prestriate monkeys. This consisted of pairs of cords arranged in various patterns, some crossed and some uncrossed, so that the monkey was supposed to see which cord had food on the end of it and pull it (see Harlow and Settlage). Lashley used six different patterns. Two of his prestriate monkeys were able to solve these problems just as well as normal monkeys, but three of them had some impairment. These monkeys, however, also had invasion of their primary visual fields, and Lashley therefore believes that their difficulty in solving the string patterns was one of visual capacity rather than "visual association."

OTHER AREAS OF THE CORTEX

It is, of course, an important question whether areas other than the striate and prestriate visual areas are necessary for form discrimination learning and retention. We have two experiments in rats that try to answer it.

Lashley has made extensive lesions all over the rat's cortex both before and after learning of a form discrimination. He has been unable to find any areas outside of the striate cortex that make any difference in the learning or retention of the habit. For that reason, he considers the striate cortex in the rat to be completely autonomous for visual functions.

Several years ago there was a report that lesions outside the striate cortex interfere with the discrimination of forms resembling an upright F and an inverted F (Kirk). After examining the anatomical data on the rats used in this experiment, Lashley believes that many of the lesions considered to be outside the striate areas did, in fact, invade these areas. Consequently, Lashley believes the retardation of discrimination in the experiment to be due to injury to striate areas and not to other parts of the cortex.

VISUAL AGNOSIA

There is a kind of visual memory that is very much like the discrimination of forms. It is knowing the meaning of various visual objects—knowing that a banana is to eat, that a bolt is not, that a book is something to read, and that a door is the way to get out of a room. Because we are not exactly sure how this kind of ability is related to the discrimination of form, we are treating it separately. Whatever it is, it is something that is frequently lost when there is damage to the cerebral cortex in man, and its loss is called *visual agnosia.* We shall consider briefly the experiments concerning visual agnosia in animals.

Prestriate Areas. When he was studying monkeys with prestriate lesions, Lashley also tried to test them for any visual agnosia. He scattered pieces of food, some small and some large, some very palatable to the monkey and others not so desirable, among a number of inedible objects, such as bolts, nuts, blocks of wood, and the like. The problem for the monkey was to pick out the edible objects from the inedible ones. Some of the prestriate animals, Lashley found, had trouble passing this kind of test immediately after operation. When they were allowed enough time for recovery, however, they were all able to pass the test. The conclusion, then, from this study is that visual agnosia does not depend upon the prestriate areas.

Frontal Areas. There has sometimes been a suspicion that some parts of the frontal lobe might be involved in visual agnosia. In one study with monkeys, in fact, Kennard reported what seemed to be a visual agnosia when the frontal eye fields (Brodmann's area 8) were surgically removed. In general, however, other investigators have failed to see visual agnosia in lesions of this type. Lashley has run three monkeys with such lesions. In two of them he found no visual agnosia, but in a third one he did. So as matters stand we have conflicting results and it is not safe to come to a conclusion.

Temporal Lobes. Although for years the prestriate and frontal areas have been suspected, it was not until recently that there was any reason to suspect the temporal lobes. It is still not certain just what parts of the temporal lobes may be important or just what aspects of visual perception they may figure in, but it seems certain that they do something.

The evidence comes from a study of several monkeys with damage to their temporal poles (Klüver and Bucy). There were a number of symptoms that went along with such a lesion—we already referred to some of them in the chapter on emotion—but most important from our present point of view was the visual agnosia. The monkeys acted as though they did not recognize common visual objects, including food. They would pick up all sorts of inedible objects, such as nuts, bolts, pieces of cement, and so on, carry these objects to their mouth as though they were going to eat them, and finally reject them only after tasting them. No extensive studies of formal visual discrimination were made with these animals. It was perfectly clear, however, that they had lost some of their ability to remember and recognize the meaning of objects.

The anatomical basis of these findings is still a bit obscure. We are not certain exactly how much and what parts of the temporal lobe are necessary for this syndrome. Most of the lesions have been rather large. Indeed, it looks as though some might have affected the prestriate regions. Certainly many of them invaded the hippocampus, which lies just under the temporal pole. It is too early to draw conclusions on this point. Now we know only that lesions in the general region of the temporal pole produce symptoms of visual agnosia.

VISUAL GENERALIZATION

Our last topic in this chapter is the problem of neural mechanisms of visual generalization. Although we use the term "generalization," we might just as well have said "equivalence," "transfer of training," "spread of effect," "similarity," "proaction," or "retroaction." All these terms refer directly or indirectly to the fact that once we have learned to respond to a particular stimulus, we may continue to respond in the same way to somewhat changed stimulus conditions. There is no need to go into the general theory and definition of these terms—we are using them loosely anyway—but the interested reader may consult Lashley or Klüver.

INTEROCULAR TRANSFER

There is one aspect of visual generalization that is so obvious that most of us overlook it. How is it that we recognize a visual stimulus even when it falls upon different parts of the retina? Or perhaps on the retinae of different eyes? We can recognize people and objects 'out of the corner of our eyes' even though we first learned to recognize them by seeing them with our foveas. We can, of course, learn to recognize something using only one eye and then recognize the object perfectly well when we see the object with our other eye. What is the physiological basis of this kind of ability?

Rats. One can tackle this problem by training animals to make a visual discrimination with one eye blindfolded, then test them with the other eye blindfolded under a variety of experimental conditions designed to get at the physiological factors in the situation. This kind of experiment has been done with both the rat and the pigeon, which represent two typically different visual systems. In rats, the optic nerves partly cross at the optic chiasma. The two eyes are both represented in each side of the brain. In fact, they send fibers to points that overlap each other. In addition, there are other connections within the visual system, which we shall come to in a moment.

In one experiment with rats, the crossed fibers of the optic chiasma were cut and the uncrossed fibers were left untouched (Levine). In this way fibers from the left eye went only to the left side of the brain and those from the right eye went only to the right side of the brain. Animals prepared in this way and having one eye blindfolded were trained to make a discrimination. They were then tested with the other eye blindfolded. The result was perfect retention, *i.e.*, perfect interocular transfer.

But the trouble with this experiment is that it does not consider the connections from one visual cortex to the other via the corpus callosum. In the many studies that have been carried out, the corpus callosum does not seem to be good for much, but it is possible that it figures in such functions as interocular transfer. In another experiment, therefore, the same kind of training and testing was done with animals in which the posterior part of the corpus callosum had been sectioned (Lashley). In this case, as in the section of the optic chiasma, there was interocular transfer. The only trouble was that the animals in which the corpus callosum was sectioned were different animals from those in which the optic chiasma was partially sectioned. We end up, then, without a crucial experiment, *i.e.*, one that cuts all crossings of the visual system. We cannot therefore draw any firm conclusions. We know only that neither the optic chiasma nor corpus callosum is solely necessary for interocular transfer.

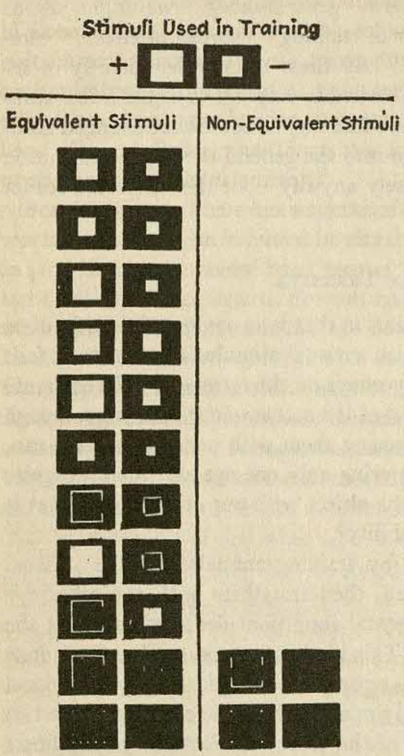

FIG. 157. Examples of equivalent and nonequivalent stimuli. Monkeys were trained to choose the left member of the uppermost pair of stimuli. They were then tested with other pairs and showed a preference for the left-hand member of each pair marked equivalent but no preference for either member of the pairs designated nonequivalent. (*From H. Klüver. Behavior mechanisms in monkeys. Chicago: University of Chicago Press,* 1933. *P.* 175. *By permission of the publishers.*)

Pigeons. In birds, however, the problem of interocular equivalence has received a more definite answer (Levine). Pigeons trained to discriminate patterns, color, or brightness show interocular transfer under some conditions and no such transfer under others. When the patterns are placed directly in front of them and they are trained while using only one eye, they show not the slightest indication of memory when tested while the other eye is being used. Yet when the stimuli used in discrimination are placed just beneath their heads, they exhibit perfect interocular transfer. This interesting phenomenon, it seems, is explained by the part of its visual field that the pigeon uses in its discrimination. Interocular transfer seems to occur when the binocular field is used and to fail when the monocular field is used.

It is thought, too, that only the binocular parts of each half of the visual systems—the parts that 'see' the same objects—are connected together. Fibers from the eyes are completely crossed, the main visual centers are subcortical, and there is a small commissure connecting the two superior colliculi. That much is anatomical fact. In preliminary experiments Levine cut the collicular commissure, and he reports that pigeons so operated on failed to show interocular transfer under the conditions in which he could get transfer in normal pigeons. If these experiments are confirmed, we will have evidence that interocular transfer occurs by way of the collicular commissure.

Visual Generalization in Rats. Now let us turn to some other aspects of visual generalization. We have a very thorough study of visual generalization of different forms in the case of rats learning to make form discriminations (Lashley). A great variety of different forms or patterns were used in the study, and many of the patterns had a variety of details that could be used by the rat for discriminating (see Fig. 157). After the animals had learned to discriminate any particular pair of cards, they were tested to see what aspects of the forms they were using. This could be done by testing them on a variety of forms and seeing which ones they "passed" and which they "failed," *i.e.*, which forms they consistently chose. In this way it was possible to tell what parts of various forms had been "picked out" in the original learning of the rat.

Out of this study Lashley concluded that the abstraction of certain details and the neglect of certain others is a fundamental aspect of the learning process. Some animals, he found, selected one detail, others some other detail. To sum up his results and conclusions, it is best to use his own words.

> Discrimination was found to be based upon the abstraction of certain general properties of the figure which are then recognized in nonidentical figures. Ease of discrimination depends upon the presence of certain relational properties, such as predominant direction. . . . Differences in the ease of discrimination and recognition of different figures indicate that the rat's visual system functions most efficiently in spatial orientation—the recognition of relative distance and direction—and that the identification of objects or forms, though possible, is secondary to a system of space coordinates.[1]

There is another somewhat similar study of visual equivalence of forms that was carried out later by Maier. Like Lashley, he found that rats learn different things when they have several possible cues to use in a visual pattern. In general, however, if they had the opportunity, his rats chose intensity differences to use in discrimination. They could and would sometimes use size differences independently of intensity differences. And sometimes they chose some absolute property of one of the stimulus cards.

Visual Generalization and the Cortex. After this straightforward behavioral study of visual generalization in the rat, Maier went on to study the effect of cortical injuries. He used a standard pair of cards for original learning, then constructed a series of other cards to use in tests of equivalence (generalization). From the scores on the equivalence tests he could determine what factors animals were using in their original learning. Also, the percentage of cards that were equivalent for a rat could be used as an index of visual equivalence for that rat.

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[1] Lashley, 1938, p. 187.

There were two results that stood out in Maier's study of cortical injury. (1) The equivalence scores of animals decreased simply as a function of repeated testing. That is to be expected because equivalence (generalization) cannot be run without involving some kind of learning or change of response on the part of the animal. (2) The effect of cortical injuries was to increase the equivalence reactions of the rats, an effect directly opposite to the effects of repeated testing. This increase in visual equivalence in operated animals occurred for animals whether or not the lesion was in the visual area.

In a similar but more extensive study, Wapner got similar results. Equivalence reactions were increased after brain lesions and decreased with repeated testing. He did not find any correlation between the size of the lesion and the equivalence scores (though Maier did). He was able to show that equivalence reactions were due to the rat's using some combination of intensity and size. The intensity factor became less important on retesting and more important as a result of operation.

Speaking of intensity brings us to the final experiment on generalization in rats (Hebb). In this experiment both normal and operated animals were trained to discriminate between two panels of different intensity. After learning was complete the intensities of the stimuli were changed, but in such a way that the positive stimulus had exactly the same ratio to the negative stimulus as it had before, even though the absolute values of both stimuli were considerably different. Normal animals transfer perfectly well from the old to a new stimulus situation, showing that they discriminate relative, not absolute, differences in intensity. Rats with their striate areas destroyed behaved exactly as did normal animals. The ability to generalize from one intensity to another, therefore, does not depend upon the striate cortex.

Visual Generalization in the Monkey. The only experiments of this type that we have in higher animals are those recently reported by Lashley for monkeys with prestriate lesions. In the same prestriate monkeys that we have already discussed, he ran tests of generalization of intensity very much like those we just described for the rat. There were only minor differences in method. The result was the same. Animals suffering prestriate lesions were just as good at such generalization as were normal animals.

There was one more test that Lashley ran in his prestriate monkeys. He has called it the *conditional reaction* (see also Lashley, 1938). In this test the animal learns to discriminate different forms, *e.g.*, a triangle and a circle, but if these forms are on a black background the triangle is the correct stimulus, and if they are on, say, a striped background the circle is positive. Thus the reaction to a pair of stimuli is "conditional" upon the background.

Unfortunately, the results of this kind of test of generalization were not consistent. Two of the prestriate monkeys had no difficulty with the test. The other three monkeys of the study, however, showed definite deterioration of ability to remember or to relearn the discrimination. Why there were such differences between the animals is not clear. There is nothing in the nature of the lesions to make us believe that certain lesions were more damaging than others (Lashley). Again we have to let the problem rest by saying that more research is needed to clear it up.

CHAPTER XXIII

PROBLEM SOLVING

This is the last of three chapters on learning. It is hard to explain just how its subject differs from the other two chapters, and we shall not try very hard. Certainly we do not yet know enough about learning to make clear-cut definitions of different kinds of learning processes. In the main, what distinguishes this chapter from the others is the methods used in the research to be considered. In conditioning studies a subject gives a signal, like raising a paw or a finger, for the presence or absence of a stimulus. In discrimination he indicates his choice, by running or reaching for different objects, between two or more stimuli. In problem solving the stimuli are not so well defined. Neither the experimenter nor the subject may ever know what particular cues are being used to solve the problem. The main thing is that the subject does something. He runs through a maze, discovers a lever to push, learns to use a rake to pull in food, or does several different things in a particular order. In any event, by trial and error he learns to do something that gets him some reward, say, food. That, briefly, is what we mean by problem solving.

Kinds of Problem-solving Behavior. Research workers have devised an endless variety of problems to give animals and human beings to learn. These problems can be classified in several different ways. One way is in terms of locomotor vs. manipulative problems. In locomotor problem solving the animal moves about in space and solves its problem by finding out the correct way to run or climb or walk. In manipulative problems the animal or human subject stays fairly well put but must learn in some way or other to manipulate a latch, string, or stick in order to solve the problem. Because rats, as well as animals below them in the phyletic scale, have poorly developed manipulative ability, most of the problems we give these animals to do are locomotor problems, such as mazes, runways, or very simple pedal boxes. Conversely, in monkeys, apes, and man, all of whom have highly developed manual skill, the typical problem is a manipulative problem.

Another way to distinguish different kinds of learning problems is in terms of the cues available for solution. In mazes and simple problem boxes there is always some external cue in the situation which will tell the subject what to do next, if he will but discover the cue and use it. In many problems devised for both rats and human beings, however, all the cues for solving the problem are not immediately available in the situation. Instead, the subject must remember what he has done some time before in order to pick the right response at any particular time. Or he must use reasoning and imaginative processes to get the solution.

In the material that follows, we shall present examples of these various kinds of problems and tell you, as far as present research will allow us, on what physiological mechanisms the ability to learn and retain these different kinds of problem solutions depends.

MAZE LEARNING

The maze is one of the earliest instruments to be devised for studying animals. It is relatively simple to construct, it can be made in a variety of ways, and its difficulty can be varied by changing its pattern or increasing the number of alleys in the maze. For these reasons it also became one of the first instruments for the study of the function of the brain in learning (Lashley and Franz). Surgical lesions were made in rats' brains both before and after learning a maze to see what effects they have on learning and retention of maze habits. We shall review the facts and the interpretations of such experiments.

BRAIN LESIONS AND MAZE LEARNING

Actually, there have been many different sorts of physiological experiments with maze learning. All of them used rats. Some involved deprivation of the senses, others cut parts of the spinal cord, and others attacked different parts of the brain. We shall come to all of them in due course. Let us begin, however, with the effects of brain lesions upon maze learning and maze retention. This topic leads to questions that will later bring up other kinds of experiments.

The Cerebral Cortex. There are a host of experiments in which some part of the cerebral cortex has been removed and the maze learning of a rat has been measured. Most of these experiments have been carried out by Lashley, although others have done some, too (see Lashley and Wiley). The general procedure has been to destroy areas of the cortex before and after learning has taken place. In the principal experiments, Lashley used mazes having three steps of difficulty. One maze, Maze I, had only one blind alley; a second maze, Maze II, had three blind alleys; and the most difficult maze, Maze III, had eight blind alleys.

Learning. The results of the experiments are depicted in Fig. 158. As you might guess, the effect of cortical lesions on ability to learn and to remember a maze habit was greater for Maze III than for Maze I. For the simplest (one-blind-alley) maze, small or moderate lesions of the cortex did not affect the rate of learning of the maze. But quite large lesions destroying, say, 50 per cent of the cortex did have some deleterious effect on rate of learning. In any case, the place of the lesion in the cortex has nothing to do with whether the learning rate was impaired. Only the size of the lesion was important. The relationship between size of lesion and impairment of learning rate can be put

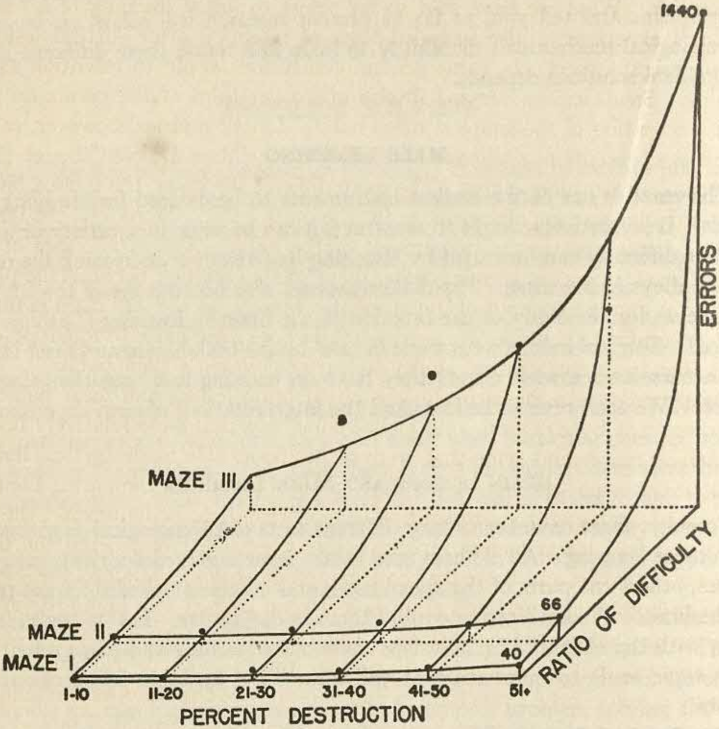

FIG. 158. A three-dimensional graph of the results of a cortical lesion showing the relationship between the size of the lesion, the difficulty of the maze, and the degree of retardation resulting from the lesion. (*After K. S. Lashley. Brain mechanisms and intelligence. Chicago: University of Chicago Press,* 1929. *P.* 74. *By permission of the publishers.*)

in statistical terms as a correlation of .20. This, you will recognize, is a small correlation. It was significant, however.

The correlation is considerably higher for Mazes II and III, the more complex mazes. For Maze II, the statistical correlation between size of lesion and rate of learning was .58. For Maze III, it was .75. So the degree to which cortical lesions interfered with rate of learning was proportional to their size. Where they were located was not important.

The upshot of the series of experiments with the three mazes and with lesions before learning was this: (1) the rat's ability to learn any of the mazes does not depend upon any particular area of the cerebral cortex; (2) in general, learning ability after cortical lesions is proportional to the amount of cortex left intact; and (3) the relation between mass of cortex and maze-learning ability is more predictable—the correlation is higher—the more difficult the maze to be learned.

Retention. What we have said so far refers to initial learning of a maze. Lashley's experiments also included tests of retention after cortical lesions. As you might expect, the same general conclusions apply to retention as to learning. Small lesions varying in size up to one-third of the cortex do not disturb retention of the simplest maze habit. Larger injuries, however, cause some loss of retention in the one-blind-alley maze (Maze I), even though they do not impair learning ability. The more difficult the maze, the more a lesion of a particular size impairs memory for the maze habit. Moreover, the larger the lesion, the greater the impairment of the habit. And in all cases of retention tests, just as in learning tests, there was no relation between the place of a lesion and the amount of impairment. Finally, as the last main point of these experiments, a lesion of a particular size does more harm to retention of a habit already formed than to ability to learn or relearn a maze habit.

Closely related to these conclusions about brain lesions and maze habits is an experiment by Erickson. He picked some rats that were relatively bright in learning mazes and some that were rather poor. He made cortical lesions of about the same size, *viz.*, 20 per cent, in all of them. In comparing the preoperative learning with postoperative tests of retention, he found that the animals that had learned most rapidly before operation remembered the most after the operation and those that had learned most slowly retained the least—although both bright and dull animals had been trained to a high criterion of performance before the operations. The conclusion, then, from Erickson's experiment is that, other things being equal, the effect of cortical lesions upon memory is less in bright rats than in dull ones. Or put another way, intelligene rats seem better able to go without some of their cortex than dull rats.

Subcortical Mechanisms. Just as Ghiselli and Brown looked into subcortical mechanisms in discriminative learning (page 469), they have done it in the case of maze learning. With the stereotaxic instrument that let them make lesions in the thalamus and midbrain with relatively little damage to the cortex, they compared the learning of rats with subcortical lesions with that of normal rats. Their results showed little harm came from lesions in the anterior nuclei of the thalamus. These, we know, are connected with the hypothalamic-amygdaloid-limbic system (see page 352), which probably has more to do with emotion than with learning. Of the other thalamic nuclei, injury to any seemed to impair learning ability somewhat, but the most important of all were the sensory and association nuclei—which make up the greater part of the thalamus. Although no statistical correlations were run, the mass of the subcortical lesion correlated fairly highly with the amount of impairment of learning ability.

Mass Action. You see in these experiments with brain lesions and maze learning a fact that will appear again in other studies to be taken up later. This fact is that neither the learning nor the retention of a maze habit is localized in any specific area of the cortex. Instead, the degree of retardation in learning or of loss of memory following cortical lesions is proportional to the amount, not the place, of the cortical lesion. This fact—called mass action—has been demonstrated over and over again. There can be no question about it. The only question is, What does it mean?

MASS ACTION AND MAZE LEARNING

We are not, at this time, going into all the theoretical problems that this question raises. We shall simply point out three different possibilities for understanding the fact of mass action and give you the experimental evidence bearing on each one. The first of these is that there is a *general mass factor* in learning ability, that the facts mean just what they say, *viz.*, learning is a function of the whole cerebral cortex. The second possibility is that learning is made up of a number of specific processes which depend on their specific systems in the brain but that these systems are so dispersed and so overlapping in their arrangement in the cortex that we cannot sort them out with maze experiments. This we might call the possibility of *dispersed specific factors.* The third possibility goes like this: there are a number of specific sensory cues involved in maze learning; the learning processes connected with each cue are localized in some part of the cortex; however, we find mass action, not localization, in the maze experiments because we are disrupting only a certain proportion of the cues used in maze learning. We may call this the possibility of *localized specific factors.* Let us now consider the experimental evidence bearing on these three possibilities.

General Mass Factor. To test the first possibility, that a general mass factor might play some part in the phenomenon of mass action, Tsang devised some experiments in which he compared the effects of removing the visual cortex with those of blinding rats. If mass per se is a factor operating in maze learning, he argued, the animals with cortical lesions should be more affected than those which are blinded. And that was exactly his finding in his first experiment. He showed that removal of the visual cortex in addition to blinding caused more retardation than blinding alone. In another closely related experiment he found that removal of the visual cortex alone caused more retardation in learning than simply blinding the animals. These results, he concluded, were definite evidence for a general mass factor in the cortical processes of maze learning.

There are some questions to be raised about Tsang's data, however. In his effort to remove completely all the striate cortex he made relatively large lesions, which, on the average, invaded other cortical regions in addition to the striate area itself. We do not yet know just what these areas outside of the striate area do. Electrophysiological evidence indicates that they are auxiliary visual areas of some sort (Fig. 152). Indeed, they seem to be homologous with areas 18 and 19 of the primate cortex, which apparently are concerned with a system of spatial coordination that is tied in with vision but not restricted entirely to vision (Fulton). So there is the possibility that the greater effect of striate lesions in Tsang's experiments was due to the involvement of other areas which have their own specific functions in learning.

To control this possibility, Finley repeated Tsang's experiments. In doing so she made sure not to make lesions outside of the striate area. Since cortical operations in the rat are by no means precise, the result was that most of her operations did not take out all the visual area. Thus, though the visual cortex includes about 20 per cent of the rat's cortex, her lesions averaged only about 10 per cent. Tsang's previous lesions had averaged substantially more than 20 per cent. Finley found no mass action. In fact, her rats with cortical lesions got along better in maze learning than did blinded rats. And in experiments in which visual cues were not necessary for learning the maze (in the dark), her animals with cortical lesions were just as good as the normal animals.

That might seem to settle the issue of the general mass factor, but it does not. Lashley, not satisfied with Finley's results, has done the experiment over again, this time making his lesions smaller. He again found positive evidence of a mass factor in the visual cortex. But again his lesions were too big. Though not so large as in Tsang's previous experiment, they averaged slightly more than the area of the visual cortex, and many of them ran well over into adjacent areas.

As matters stand at present, it is not possible to make a final decision about the existence of a general mass factor of the cortex in maze learning. Further experiments are called for. It would be helpful if we knew about the functions of areas adjacent to the visual cortex. That might give some clue as to whether running lesions over into these areas is responsible for the difference in results. Lashley thinks not. Another possibility is a comparison of lesions of approximately the same size made entirely within the visual area with those made adjacent to the visual areas. In this way we could see whether lesions extending into adjacent areas, although of the same size, impair learning more than those within the striate area. Specific comparisons of this sort have not yet been made.

Dispersed Specific Factors. It is no easier to test the hypothesis of dispersed specific factors than to test that of a general mass factor. There are, in fact, no experiments that bear on it directly. There are only some well-known facts that let us believe that such factors could be at work, at least within certain limits.

In the rat, the electrostimulable areas (see Fig. 159) spread out over a large part of the cortex. Indeed, they cover most of the anterior half. So the area concerned in strictly motor functions is of considerable size. The somesthetic sensory projections, similarly, although not perfectly delimited, cover a rather sizable portion of the lateral and dorsal surface. Little is known of the extrapyramidal areas of the cortex, but in the primates these are distributed over a large section of the cortex, consisting chiefly of the premotor areas and the parietal areas. In view of the encephalization that takes place in other respects between rats and primates, they can be no less dispersed in the rat. Thus, from the dispersal of these three different systems, it is easy to see that cortical lesions are not likely to eliminate any one of them discretely, should one of them be more important in learning than another. Then if it be granted,

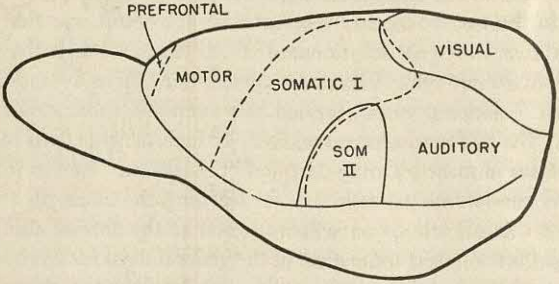

Fig. 159. Lateral view of the motor and sensory areas of the rat's cerebral cortex. The sensory areas were obtained by taking electrical records from the cortex during stimulation. The motor area was mapped by finding the points that were electrically stimulable. (*After LeMessurier and Woolsey, personal communication.*)

as seems reasonable, that several such systems are concerned in such a learned behavior as the maze habit, it would really be quite unexpected if learning were related to cortical functions in any but a purely statistical way, *i.e.*, in the manner seen in mass action.

Localized Specific Factors. A large part of the fact of mass action is undoubtedly to be accounted for on the basis of the great number of specific factors involved in maze learning. Assume, for example, that in solving a maze an animal taking its route through the maze uses several different sensory cues at various times. Assume also that the nerve networks through which it learns a response to a particular cue are located in some sensory area of the cortex. Then the more cortex one removes, the more of these connections will be destroyed, and the greater will be the deficit in maze learning or retention. Or assume, similarly, that some animals mainly use one sensory cue and that other animals mainly use some other type of cue. Yet the experimenter does not know which animal is which. Whether or not a lesion damages the particular area mediating the learned response in each case becomes then a matter of probability, and the greater the size of the lesion, the greater the likelihood of destroying the area through which learning takes place. In either case we might expect learning and memory for maze performance, as studied in the experiments described earlier, to look as though it does not depend upon a particular place in the cortex but rather on mass.

Both these assumptions are bolstered up by experiments. It is known, in the first place, that animals vary among themselves in the cues of which they make use in solving maze problems. One way of testing that is to remove different cues, after an animal has learned a maze, and see what effect this procedure has on his memory. In experiments in which rats were trained in the light and subsequently tested in the dark, for example, some animals were considerably disturbed and others were not (Dennis, Finley). Another test is to provide two different solutions of a problem, one employing visual cues and another positional ones (tactual-kinesthetic). In this case some rats take one 'hypothesis' and other animals the second 'hypothesis' (see below).

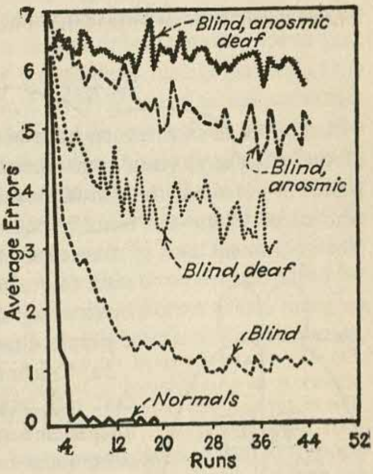

FIG. 160. The effect of sensory deprivation upon maze learning. (*After Honzik. From L. W. Crafts et al. Recent experiments in psychology. New York: McGraw-Hill,* 1938. *P.* 147. *By permission of the publishers.*)

The second assumption, you will remember, is that cortical lesions of increasing size deprive the animal, in increasing amounts, of necessary sensory cues. This can be tested by studying the effects of the destruction of sense organs upon learning (see Munn). Here one finds results essentially comparable to those of mass action (see Fig. 160). If animals are blind while learning a maze, the lack of vision has little or no effect upon their learning. The same is true if one destroys the olfactory bulbs. Combining anosmia and blindness, however, makes a great deal of difference; animals are appreciably retarded in their learning of maze problems. It is a little difficult to make more extensive combinations, but even this result points rather definitely to the conclusion that in sensory deprivation, as in cortical destruction, there is a 'law' of mass action. In the former case, however, it is plain to see that no mass factors are concerned, but on the contrary only specific sensory factors.

SELECTION AND VARIABILITY

We have not heard the last of the problem of mass action. There will be more of it in the sections that follow. In fact, what we are going to talk about now will throw some more light on the problem. We must, however, shift our frame of reference a bit and look at learning a little differently. Instead of thinking of animals as passive subjects in a learning experiment, who come through trial and error or through conditioning to give the correct responses, we shall think of the animal (or human) subject as doing some 'choosing' and 'hypothesizing' in the course of learning. As we shall see, animals do not always make use of all the cues in a learning situation but select one or another to use. They also do not always make all possible responses but sometimes use one, sometimes another. These aspects of the learning process, the selection of cues and the varying of behavior patterns, have been subjected to some physiological experimentation, and that is our subject here

SPATIAL VS. VISUAL HYPOTHESES

A number of experiments have been so arranged that we can find out which of two cues, say, visual and spatial cues, a rat uses in a particular learning problem. Most of these studies were done by one investigator, Krechevsky, who chose to use the term 'hypothesis' in describing this selective behavior. The instrument used in these experiments was a maze, made in four units from start to goal box. The rat could solve the maze either by entering all lighted alleys (visual cues) or by using a simple directional tendency (spatial cues).

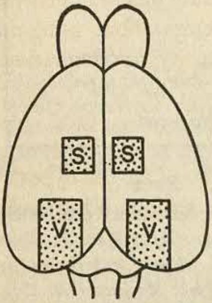

FIG. 161. Areas for hypotheses in the rat. The removal of area *V* abolished visual hypotheses, and the removal of area *S* abolished spatial hypotheses. (*After Krechevsky,* 1935.)

In Krechevsky's first experiment he demonstrated that rats tend to have different hypotheses in running such a maze. Some react consistently to spatial cues, some to visual cues, and some use both. This could be determined by analyzing the pattern of turns made by the animal on each trial in the maze. It is interesting to note in passing that when a bright strain of animals was compared with a dull strain in this hypothesis behavior, the dull animals were the ones who used visual cues the most extensively.

'S' and 'V' Areas. The next question (and an interesting one) was the effect of cortical lesions on such hypotheses (Krechevsky). Lesions of various sizes were placed at different locations on the cortex so that the whole cerebral cortex was explored. The conclusion: cortical lesions reduce the number of hypotheses in rats. Whereas normal animals tended to use both visual and spatial hypotheses and to vary from one to another, animals with cortical lesions were inclined to take one hypothesis and stick to it. The reason for this became clear when the brains were studied anatomically (see Fig. 161). It turned out that a cortical area corresponding fairly exactly with the striate (visual) area was responsible for the visual hypothesis. When it was removed, animals shifted to the use of spatial hypotheses. On the other hand, an area a little in front of center on the cortex was crucial for spatial hypotheses; animals with this area removed preferred to use visual hypotheses. This is a simple result that is easy to understand.

Mass Action. This same maze used for studying hypotheses can also be used to study the learning of a type of intensity discrimination simply by arranging the lights over the correct alleys and by eliminating spatial cues. Two investigators have done that (Krechevsky, Ghiselli). One used small lesions of about 10 or 12 per cent, in most cases overlapping the visual area. The other used considerably larger lesions (up to 55 per cent) distributed over the entire surface of the cortex. The strange thing is that both investigators found that the lesions interfered with the learning of an intensity discrimination. It is strange because in Lashley's studies, using a discrimination technique rather than a maze technique, lesions in the cerebral cortex, even those covering the entire visual area, did not impair the learning of an intensity discrimination. Even more interesting was the statistical analysis of the effects of the larger lesions (Ghiselli): there was a correlation of about .80 between retardation in rate of learning and the size of the cortical lesion, and the location of the lesion was of no importance. Mass action again! Why this result was obtained we do not know. Apparently there is something quite different about using an intensity cue to learn a maze and learning a simple intensity discrimination.

SPATIAL HYPOTHESES

There are other studies dealing with the brain mechanisms of spatial hypotheses. These do not use the four-unit maze but employ various other techniques.

Variability. One was a 'block maze' in which there were several different routes to the goal, all correct and all of the same length (Krechevsky). Errors could be made only if the animal turned away from the general direction of the goal box or entered a blind at the side of the maze. Normal animals were compared with animals (rats) suffering lesions of different sizes in various parts of the cerebral cortex. The normal animals took many more different paths—nearly twice as many—than did the operated animals. Normal animals also shifted from one path to another—they were run only one trial each day—much more than did the operated animals. Thus the number of hypotheses was cut down by the cortical operations. The degree of these decreases was correlated rather highly with the size of the cortical lesions (r = .37 to .67). Mass action again!

Single Alternation. Quite similar in principle to this last study is one on the simple alternation behavior of the rat (Morgan and Wood). The investigators ran rats in a simple T maze with rewards on both sides and counted the number of times the rats alternated between right and left choices. Normal animals, as has been demonstrated several times, take alternate paths about 80 per cent of the time (Dennis and Sollenberger). Some operated animals cut down their variability considerably and consistently chose either the left or the right path. Post-mortem examination of the lesions indicated some localization of function. All animals with lesions in the frontal areas adopted the stereotyped behavior, some animals with parietal lesions did too, but animals with occipital lesions in the vicinity of the striate cortex continued a high degree of alternation.

Variable Paths. Krechevsky has done some more experiments on the problem of variability of spatial hypotheses. In one of them he ran rats in an apparatus where two paths to food were available. One was a variable path through a block maze similar to the one described above; the other was a standard path involving turns in simple alternation. On each trial the animal was permitted to choose either the standard path or the variable path. Taking the variable path in this case was no particular advantage or disadvantage in getting the food reward. Normal animals, Krechevsky found, tended to vary their responses more than do operated animals. They chose the variable path about 50 per cent of the time and the standard path about 50 per cent. The operated animals, though they started out in the first few trials about 50-50, gradually reduced their choices of the variable path to about 20 per cent, taking the standard path 80 per cent of the time. Even minor cortical injuries seemed to cause this stereotyping of behavior. No correlation, however, between the size of the lesion or its locus and any of the measures of variability could be found.

Because he was concerned that the standard path was about the same length or perhaps shorter than the variable path and this might have something to do with the results, Krechevsky ran another experiment. This one was identical with the one before except that the standard path was longer by a ratio of 1.54 than the average variable path. In this case his operated animals did not develop the preference for the standard path. They were, however, less variable in their choices than the normal animals and tended to perseverate on one choice longer than the normal animals. He obtained a correlation of $-.36$ between the size of the cortical lesion and the number of times the variable path was taken; also he found an r of $-.59$ between size of lesion and variability in the choices of the animal.

Umweg Behavior. Somewhat different but still related to spatial hypotheses is a study of umweg behavior and brain lesions (Krechevsky). The apparatus in this case was so constructed that the rat had to make an intensity discrimination at the first choice point, taking the path toward the light. Up the path, however, the rat could choose again, this time between a long spiral path along which the food and the light were always visible and a short path through a tunnel directly to the food. This short path was psychologically the *umweg*, or roundabout path, because the rat had to leave the field of visibility of light and food. When rats were subjected to brain lesions, they made vastly more choices of the spiral, longer path (58.9 vs. 17.1 per cent of the time). In a control experiment, however, in which the intensity discrimination was eliminated and the animals simply chose the tunnel vs. the spiral path, the operated animals chose the spiral path only 12 per cent of the time while the normal rats chose it 18 per cent. This means that the intensity discrimination presented no difficulty to the operated animals. It also means, however, that the animals operated on tended to depend on the light cue more than the normal animals.

VARIABILITY IN MANIPULATIVE BEHAVIOR

In this chapter we distinguished between locomotor and manipulative behavior. So far we have been talking only about locomotor behavior, even in the matter of hypotheses and variability. We can raise the same questions, however, about manipulative behavior as we have about locomotor behavior. There are relatively few data on the neural functions involved in the learning and retention of such behavior. Such as there are point to the importance of variation and stereotyping of such patterns in manipulative learning.

Handedness. There are two studies, worth mentioning briefly, of changes in handedness in manipulative problems. Many years ago Lashley observed that monkeys readily shifted from one hand to the other when neural injury paralyzed one side. Animals were taught a manipulative problem in which they used only one hand. The motor cortex responsible for that limb was then removed, partially paralyzing the monkey. Upon postoperative testing, the animal promptly used the other, unparalyzed limb to solve the problem. Lashley cites this as an example of equivalence in motor functions. More recently, Peterson has reported a similar phenomenon for rats. He first demonstrated that most rats show some hand preference, either left or right. He then located a point on the cortex, corresponding to the motor cortex in primates, which when injured or removed would shift the preference to the other side. Though the limb originally used was not paralyzed by the operation, it probably was made less usable.

Problem Boxes. More directly on the problem of variability in manipulative behavior are Lashley's studies of latch-box behavior in rats. He used a series of different problem boxes and taught them to a group of rats. Four of these problems were distinctly manipulative problems. They required a string to be pulled, a paper strip to be torn in the right way, and so on. One of them was a double platform in which the animal had to step on both platforms before getting food. The effects of brain lesions were different for the two types of problems. The ability of animals to learn the double-platform (locomotor) problem was not affected by cortical lesions of considerable magnitude, in fact up to 58 per cent. Rate of learning was not correlated with the magnitude of any lesions made. With other boxes, however, which required manipulative behavior, there was considerable retardation in learning with cerebral lesions.

The correlations between extent of lesion and amount of damage to the cortex ranged from .48 to .72.

It is easy to understand why lesions did nothing serious to learning in the double-platform problem. Its solution requires relatively simple locomotor behavior, no complicated hypotheses, and no adaptive skilled movements. The other boxes, however, required variable behavior of the animal, first in stumbling on the correct solution and later in developing specific reactions for manipulating latches, reducing time spent in exploring particular items in the situation, and reasonably good sensory-motor coordination. It is reasonable, therefore, that almost any kind of lesion might affect the behavior and reduce the possibilities of its rapid solution. Lashley's observations of his operated animals and his analysis of results convinced him that the difficulty of operated animals in the manipulative problem boxes was basically a matter of variability in behavior. The number of exploratory acts (motor hypotheses) was cut down.

SOLUTION WITHOUT CUES

We come now to a variety of learning problems that are different in many superficial respects but have one thing in common, that the cues for solving them correctly are not immediately available to the subject. In most cases the learning problem was designed to make the subject put together items from his previous experience or to remember something he has just done if he is to solve the problem successfully. Most of these problems were specially devised to study 'reasoning,' 'thought,' or more generally speaking, 'symbolic processes.' For the time being we shall avoid the question of whether the problems actually do that and shall simply describe what the problems are like and what happens when certain parts of the nervous system, usually the cerebral cortex, are removed.

Reasoning in Rats. Several years ago one investigator devised a problem for rats that he considered involved reasoning ability (Maier). Other research workers have raised the question of whether the problem actually involves reasoning in the sense that we use it in human behavior. At any rate, normal rats can solve the problem—at least they can a good percentage of the time—and this problem has been investigated in relation to cortical functions. The problem is this: Rats are first allowed to explore thoroughly a three-table arrangement until they have become thoroughly familiar with all parts of it. Then they are allowed to feed on one of the three tables. Afterward they are placed on one of the other tables. Screens prevent the animal from seeing where the food is or where he has just been. The rat must put together his general knowledge of the maze with his previous experience of feeding on one table, in order to go immediately to the correct table.

Upon subjecting rats to cortical lesions, Maier found that they could not solve the 'reasoning' problem nearly as well as normal rats. Very small lesions of less than 10 per cent of the cortex did not make much difference in the 'reasoning' ability. Lesions between 10 and 18 per cent, however, substantially reduced ability to solve the problem, and lesions greater than 18 per cent in magnitude completely abolished the ability. Important, too, was the fact that lesions did not have to be in any particular place. One lesion in one place would do as much harm as a lesion anyplace else. In this respect Maier got another case of mass action. Indeed, relatively smaller lesions did more harm to ability to solve this 'reasoning' problem than much larger lesions do to maze-learning ability.

The Delayed Response and the Prefrontal Lobes

Another type of problem that has been devised to study problem solving in the absence of external cues is the delayed response. In this problem an animal must, after some considerable delay, make a correct choice based upon seeing the correct answer before the delay. Unlike most of the research we have been talking about in this chapter, the delayed-response problem yields a fairly clear picture of localization in one part of the brain, the prefrontal lobes. Moreover, most of the work has been conducted with monkeys, who are primates much more closely related to man than is the rat. Research on the delayed response and the prefrontal lobes has now been so extensive that the problem is a story by itself—a story we shall now detail briefly (see Jacobsen).

The Delayed Response. The studies of Jacobsen with the delayed-response problem given before and after ablation of the prefrontal lobes have now become classics in the field. In his work monkeys were shown where food was hidden under either the right or the left one of two cups. Then they were forced to wait several seconds before they could reach for the cup, remove it, and get food. Jacobsen's findings were very simple. Normal monkeys could delay for 30 sec. without much difficulty and then select the correct cup. Monkeys with bilateral lesions of the prefrontal areas, however, could not solve the delayed response if required to delay more than one or two seconds.

Localization of Capacity. As soon as these facts were known, Jacobsen and his colleagues tried to make sure whether other areas of the brain or just the prefrontal areas are needed for the capacity to make delayed reactions (see Fig. 162). They discovered that lesions of the temporal lobe did not impair the delayed reaction (Jacobsen and Elder), nor did motor or premotor lesions (Jacobsen and Haselrud). From these experiments we have concluded that the prefrontal areas, and only these areas, are concerned in delayed reactions.

Recently, however, Lashley has brought forth some unexpected results. He made bilateral lesions in the *prestriate* areas, *i.e.*, areas 18 and 19, of five monkeys. Clinical neurologists have always thought of these areas as visual association areas. The monkeys with these lesions showed full or partial loss of ability to do the delayed-reaction problem. This is especially interesting since these same monkeys did not show any disturbance of visual discriminations (see page 476). At any rate, we have the report of disturbance of delayed reaction. Until it is confirmed and until we have more experimental facts, it is too early to make any interpretation of the report.

The Memory Trace. Since Jacobsen's original studies of delayed reaction in prefrontal monkeys, research workers have bent their efforts toward finding out why prefrontal animals fail in delayed reaction. Jacobsen's own interpretation was that there is an underlying loss of *immediate memory* in prefrontal animals. Finan put this interpretation to the test. He ran prefrontal monkeys in several kinds of learning problems in which memory traces had to last some time in order for the animal to make the correct choice. In one problem monkeys had to shuttle from one grill to another several seconds after a signal was presented. In another they learned a temporal maze in which one route took a longer time than the other. Both prefrontal and normal monkeys solved these problems, though the prefrontal animals could not solve the delayed response. Finan concluded that the prefrontal monkey had no basic disability in holding memory traces. Whatever was wrong in the delayed reaction must have some other basis.

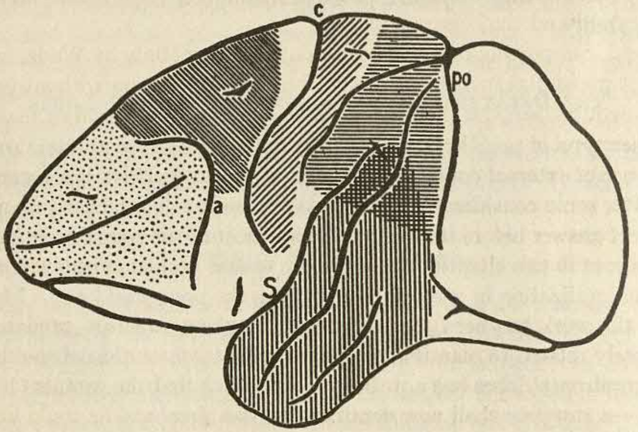

FIG. 162. Summary of the effects of cortical extirpations in monkeys upon delayed response. Extirpation of the various hatched areas had no effect; removal of the stippled area (prefrontal areas) caused permanent disruption of the capacity for delayed reaction. *c*, Central sulcus; *s*, sylvian (lateral) sulcus; *po*, parietooccipital sulcus; *a*, anterior sulcus. *(From C. F. Jacobsen. Studies of cerebral function in primates, p.* 44. *Comp. Psychol. Monogr.*, 1936, **13**, *No.* 63. *By permission of Williams & Wilkins, publishers.)*

Attentive Functions. A second possibility is that prefrontal animals have difficulty in establishing the 'correct connection' in the delayed-response situation, that they do not note well where the food is placed to begin with and therefore have nothing to remember during the delay interval. This factor is probably not the whole story, but many experiments indicate that it is of some importance. In another study, for example, Finan gave monkeys predelay reinforcement. He let them get food in the correct place before the delay as well as after it. With this procedure prefrontal monkeys succeeded in solving the delayed-response problem. In fact, one prefrontal animal could delay for several seconds on the Jacobsen nonreinforced procedure if it first had training with predelay reinforcement. This kind of result points to a difficulty in 'attention' in the prefrontal animal, a difficulty in noting the original relation between the food and the correct cup.

Sedatives. Supporting this interpretation is another study by Wade, who was able to get prefrontal monkeys to solve the delayed reaction without predelay reinforcement by keeping them under light sedatives (nembutal or dial) while working the problem. The sedative apparently slowed the animal down and let him pay more attention to the placing of the food under the correct cup. At any rate, prefrontal animals under sedative could solve the delayed-reaction problem. Again, as in Finan's case, one of the animals was able to continue solving the problem after it was returned to the normal procedure without sedatives.

Matching from Sample. Another experiment using, in effect, predelay reinforcement, by Spaet and Harlow, also showed positive solution of the delayed-reaction problem by monkeys. In this case a matching-from-sample technique was used. A sample object was presented to the animal and he could find food under it. After the delay two dissimilar objects were presented, one like the sample. The prefrontal animal, like the normal one, could pick the correct object. This again points to the ability of the monkey to solve the problem if he is made to pay enough attention to it.

No Reinforcement. Although Jacobsen's original results have been confirmed many times, it is possible, apparently, for some monkeys to solve the delayed-reaction problem without predelay reinforcement and without sedatives. Campbell and Harlow report that two out of six prefrontal monkeys were eventually able to solve a delayed reaction when the investigators used a method essentially the same as the original Jacobsen technique.

Intervening Darkness. A final experiment to bring up is one by Malmo, which also points to some disturbance in attention in prefrontal animals. He used the Jacobsen technique (no predelay reinforcement) but shut off all lights in the room during the delay interval, then turned them on again at the end of the delay. Under these conditions prefrontal animals could solve the problem. This again points to a disturbance of attention rather than of memory per se.

Conclusions. In fact, all these results seem to call for the interpretation that the prefrontal monkey has difficulty with attention. More specifically, it would look as though there is greater interference from other stimuli and other processes than in the normal animal. Anything that cuts down distractibility or interference, like shutting off the lights or slightly drugging the animal, increases memory. Or anything that combats interference effects and forces attention to the task, such as predelay reinforcement, assists memory.

That there are disturbances in attention in prefrontal animals is shown in several other types of experiments. In visual discriminations, for example, prefrontal animals can learn and master all ordinary discriminations, yet they show some signs of deficit (Harlow and Dagnon). A thorough analysis of their performance on visual discriminations indicates that they make more errors than normal monkeys. Then, when one attempts to reverse the problem—make the correct stimuli incorrect and vice versa—prefrontal animals make more errors than normal ones in a ratio of about 4:1.

To be mentioned finally is a rather simple test which also indicates difficulty in attention (Harlow and Johnson). It was almost a reaction-time test. A piece of food was exposed to the animal for a given number of seconds; if he did not take it in the time allowed, he lost it. Both normal and prefrontal animals can make the response in all reasonable time intervals, but there is a considerable difference when the interval is just 1 sec. Normal monkeys can react in 1 sec.; prefrontal animals cannot.

OTHER MEMORY FUNCTIONS OF THE PREFRONTAL AREAS

There are several other kinds of memory functions that have been studied in relation to the prefrontal areas. Both rats and monkeys have been used as subjects. It is hard to interpret the findings because the details of the various problems are different and we do not know how to break them down into the psychological factors involved in each of them. It is well, therefore, not to attempt an interpretation but simply to review the facts.

Delayed Alternation. There are two experiments in which delayed alternation has been studied. In each of them the correct response for the rat, after a delay of several seconds, was to make a turn opposite to that made before the delay. In an experiment by Loucks, the capacity for delayed alternation survived cortical lesions in the middle and posterior parts of the rat's cortex, but it was abolished by lesions in the frontal third. In a more recent experiment, taking advantage of these spontaneous alternations of rats, a similar result was obtained (Morgan and Wood). Lesions in the prefrontal cortex always reduced considerably the capacity for delayed alternation, whereas those in the back part of the brain did not.

Anticipatory Functions. Another experiment with rats shows the localization of some sort of anticipatory function in the prefrontal regions of the rat's cortex (Stellar *et al.*). The rats were run in a maze consisting of a long runway from which six alleys led off to the left. The rats were supposed to turn left at the fourth alley to obtain food. The maze was rotated in the room from time to time in order to eliminate the use of exteroceptive cues. Normal animals and animals with lesions in various parts of the cortex were run on the problem. While the interpretation of the results is not entirely clear-cut, the removal of prefrontal areas damaged capacity to solve this problem most severely and most consistently. In another experiment (Epstein and Morgan), lacking control lesions in other parts of the cortex, prefrontal rats showed a consistent and complete loss of the anticipatory goal gradient whereas the goal gradient of speed-of-locomotion was not affected (see Hull).

Complex Problems. In some of the studies on prefrontal functions in primates, learning problems have been used in which more than one act must be performed in the correct sequence in order for the animal to solve the problem (Jacobsen *et al.*). In one problem, for example, the animal is required to pull a rope, push a lever, and undo a latch, in that order, to secure a reward. In another he is required to respond to three different platforms in the correct order to be rewarded. In a third the monkey must use a short rake in order to secure a longer rake to enable him to pull in food placed at a distance outside his cage. The problem may be compounded in complexity by increasing the number of rakes that must be obtained successively in order to get food. The results on all these problems can be summarized very simply: the animal with bilateral extirpation of prefrontal areas is unable to solve them. The prefrontal monkey can learn to perform the individual acts necessary for the solution, but it cannot perform them in the correct order when a series of them is required for solution.

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CHAPTER XXIV

BRAIN LESIONS IN MAN

In all the chapters that have gone before we have said very little about human beings. Most of our attention has been given to animals. The reason, of course, is that we know much more about animals—at least we are much more certain of what we know about them. In the end, however, our purpose is to understand the physiological basis of human behavior, and we ought to say something about it, even if briefly, before we wind up the book. That we shall do in this chapter.

Clinical Methods. As psychologists we are not interested in brain lesions nor in the anatomical areas of the brain that may suffer disease. We are interested in physiological mechanisms of behavior. To get at these mechanisms, however, we must "catch as catch can"—we must take whatever brain injuries nature provides and see as best we can what kinds of disturbances of behavior go along with these injuries. That is about all we can do, and that is why we must write this chapter around "brain lesions" rather than some special aspect of behavior.

Most of the chapter will be about memory and what happens to it when there are brain lesions. As we have already seen, however, memory is entangled with the basic sensory and motor capacities, and we will have to talk about several aspects of behavior before we get through. For the moment, therefore, let us think about behavior in general. A little later we can become more specific.

SOME FACTORS IN IMPAIRMENT

There are many sources of confusion in studying changes of behavior in patients suffering brain lesions. One is that we may never know exactly where the lesion is. Another is that we may not have seen the patient before he suffered his lesion to know just what changes in behavior to ascribe to the lesions. These are rather obvious difficulties. There are also some other important factors, which have only recently been getting proper emphasis.

Variations in Structure. One of these is individual differences in the structure of brains. Just as people have different shapes of faces and bodies, so their brains vary in both gross and microscopic structure (Lashley, 1947). The positions of the primary fissures and sulci certainly vary from one person to another. So, too, do the shapes and sizes of some of the major gyri and convolutions. Such individual differences naturally enter the clinical picture. In two different individuals, lesions that sometimes appear to involve exactly the same regions of the brain may actually involve somewhat different functional areas. If the lesions do not produce the same deficits in behavior, it may be due to individual differences in the size and shape of the parts of the brain.

Motivation. Lack of motivation may sometimes make a person act as though he had a brain lesion. At least we sometimes become very forgetful when we are tired and do not care. And, of course, we do not learn nor remember very well when we do not try to. So a loss of memory or some deficit in behavior may sometimes be ascribed to a brain lesion when all that is lacking is motivation. People in hospitals, moreover, are usually not very highly motivated—except sometimes to get out. In clinical neurology, therefore, behavior deficits due to lack of motivation have sometimes been mistakenly assigned to a brain lesion.

What complicates the picture even more is that there frequently is in people with brain lesions a lower motivation to remember or to relearn tasks. How much of the lower motivation comes from being in a hospital or under medical care and how much is due to the lesion is not always clear. At any rate, motivation is frequently lower and affects the apparent impairment of behavior. Lashley tells the story of a patient, for example, who seemed to have lost a good deal of memory for language after a brain operation. The hospital staff, in fact, was trying to teach the patient the alphabet again. After 900 repetitions the patient was still failing. All he needed, however, was a little incentive, for when offered a bet of some cigarettes that he could not learn the alphabet, he promptly learned it perfectly in 10 trials and remembered it until he collected his bet. Many other examples of this sort of thing could be cited. The main point is that whether or not a brain lesion seems to produce an impairment in behavior can depend quite critically on the motivation of the subject.

Functional Duplicates. There is the fact, too, that almost any deficit in behavior after a brain lesion may also show itself in functional states (Nielsen). Stage fright may make a person just as speechless as he sometimes is after certain brain lesions. In some of the postepileptic states we see people unable to understand written or spoken language, just as though they had severe lesions of the brain. In hysteria and neurotic disorders we sometimes see cases of inability to recall names of familiar persons or objects—the same kind of inability that occurs in some brain injuries. It is, in fact, possible by suggestion and hypnosis to duplicate most of the syndromes of impairment that occur in brain damage (Teitelbaum).

If, then, we may have purely functional disorders that look like brain disorders, we obviously have lots of room for confusion and even interaction between the two. People seldom suffer brain damage without its rather seriously affecting their lives—their personal relationships, finances, employment and so on. Thus there almost certainly are functional symptoms of illness that are not directly due to the brain lesion. There are a good many cases on record, in fact, of patients suffering from some infectious disease or taking certain drugs and being mistaken for cases of brain lesion because they showed behavior symptoms classically ascribed to brain disorder.

Individual Differences. We have good reason to believe that individual differences in psychological make-up have a lot to do with the effects of brain lesions. Our evidence on this point, however, is rather indirect and not very specific. We have already seen that bright rats are less affected by lesions of a given size than dull rats (page 487), and it is reasonable to expect that this might be true of human beings. Besides general intelligence, we know that people differ somewhat in their specific abilities (Thurstone). Some are high on visual factors, others on motor factors, and so on. Individuals of comparable general intelligence may be rather different in their specific abilities. This fact can show up in the way a particular brain lesion seems to affect an individual's mental performance. We know also that there are differences in mood, motivation, and temperament that undoubtedly can affect abilities after brain lesions. Finally, as we shall see in more detail later, there is the possibility, which some neurologists hold, that individuals may differ greatly in the areas of their brains that are used and fully developed (Nielsen).

EQUIVALENCE OF STRUCTURE

We have mentioned a few factors to keep in mind in talking about brain disorders. Some of them we know little about, but they may take on more importance as research progresses. Already important, however, are several other factors, which all fall under the heading "equivalence of structure." In the chapters on learning in animals, we have seen that one part of the brain can take over the function of another part and that parts of areas can manage, after a time, to do the job that the whole area normally does. This is equivalence of structure. We shall see more examples of it as we go along. Such equivalence is an outstanding property of the brain, and it is impossible to get down to other specific problems without first taking up this topic.

Laterality of Function

The brain is symmetrical. The left side is like the right. That raises the question of the equivalence of the two sides. Do we need both sides or will one do? Do we normally use both sides or only one? If we use one and lose it, can the other take over the job? These have been important questions for a long time, and they enter into much of the behavior we see after brain lesions. To tell what we know about them we ought to start with behavior and work back to the brain. For each of the things we do most of us have a major side and a minor side. We write, throw balls, and carry objects with our right hands. A few, of course, are left-handed. Some are "switch hitters"—they can use either hand. We see right-handedness and left-handedness not only in people but also in animals (Downey; Tsai and Maurer). So there can be little doubt that *laterality*, as we may call it, is a general biological characteristic of the higher animals.

In many individuals the major side is not the same for all activities. In fact, if we get together many tests of laterality, there will be an imperfect correlation between them (see Jasper and Raney). Some, for example, prefer the left hand in writing and the right one in throwing a ball. For some the right may be the major side for the arm and hand, yet the left may be the major one for the feet or eyes. So even though there may be a general tendency for one side or the other to be the major one, there is still a good deal of variety in specific habits as to which side is major and which minor.

Laterality of the Brain. These statements about laterality of behavior are easily carried back to the brain. Voluntary behavior, we know, initiates in the pyramidal (or motor) cortex, and the pyramidal system is almost entirely crossed. If, therefore, the right arm is the major arm, the left motor cortex is the major side of the cortex, for it controls the right arm. So for many skills there is a simple 'crossover' rule.

In speech and in many sensory affairs, however, the problem is quite different. They are bilateral, not lateral, activities. The vocal cords, the tongue, and the lips are bilateral organs, which are not used in halves but rather all at once. Both sides of them work at once. In listening to sounds or in looking at objects we use both ears or both eyes as the case may be. Here the 'crossover' rule will not work. In all these cases the interesting question is whether we use both sides of our brain or only one.

We have only clinical evidence to go on, but it speaks rather clearly (Nielson; Weisenburg and McBride). Lesions on only one side of the brain sometimes disrupt speech and other memory functions. Sometimes the disruption is so great that we know the affected side has been the major hemisphere in the function. There is room to argue about how often laterality of the cerebral cortex occurs and how important it is, but there is no doubt that in some functions, particularly language, one side of the cortex is frequently the major side while the other is the minor. Later, when we take up specific amnesias and impairment, we shall have more to say about laterality and when it is at work.

RECOVERY OF FUNCTIONS

Recovery of functions is another aspect of the equivalence of structure, and it is closely related to laterality of function. In Chap. XV we have seen that there is definite recovery from paralysis that follows lesions of the motor cortex so long as these lesions are not too severe. We run into the same kind of phenomena with disorders of memory. After a brain lesion there may be great losses of memory, but memory may gradually come back in the course of time. Sometimes even after severe lesions recovery is so great that one would hardly know that the patient had had a brain injury. Such recovery has long been a problem.

Recovery and Retraining. In many cases the recovery of memory after a lesion is quite slow and there is plainly an opportunity for the patient to relearn. On the other hand, there are recorded instances of rather sudden reappearance of memories weeks or months after a brain injury knocked them out. Such sudden recoveries certainly cannot be a matter of release from physiological shock or the return of nerve cells to normal functioning. For many years now they have been the subject of much debate and theory, which we need not go into here.

Lashley has examined the records of cases that seem to illustrate these delayed sudden recoveries. He believes that they all have had some opportunity for retraining and that this is the explanation. Sometimes intense excitement of the patients helps them recover lost memories. In any event, the patients always seem to have some opportunity to practice the functions that recover. The sudden return of memory, therefore, is not a spontaneous return but rather one that follows some retraining—so Lashley holds. In some cases the retraining may be of some function that is central to a number of habits, so that practice in the function may bring back memories of many habits.

A good illustration of this last point comes from experiments with monkeys (Klüver). The monkeys were trained before operation to make various sensory discriminations. In these discriminations they reacted by pulling a string attached to the 'correct' box. After relatively small lesions in several different areas of the brain, the animals appeared to have a complete amnesia for all the habits. They pulled in strings and boxes at random, no matter what discrimination was asked of them. The forgetting, however, seemed to be a general affair—one of 'comparing' and 'choosing' between two stimuli—rather than loss of a specific habit. When the animals were retrained on just one of the discrimination habits, they were able without any more training to make the other discriminations that they seemed to have forgotten after the operation.

Mechanisms of Recovery. Whether memories come back slowly or rapidly or whether they return singly or all together, one conclusion is sure: there is a change in the function of the brain in the course of recovery of memories. If a brain lesion destroys a memory, it means that the memory must somehow depend upon the area destroyed. If after the lesion the memory comes back, it means that the memory now depends on the parts of the brain left uninjured. The question is how this change of function from one part to another comes about.

Neurologists have struggled with the question for a long time. Their answers fall into two general categories. One is *vicarious function.* This is the answer that almost any part of the brain can take over a function if necessary—can function in place of an injured area. Because an entire system, such as the motor cortex or the visual centers, may seem to be destroyed without preventing some recovery of function, it has often looked as though the various parts of the brain could take over almost any function, *i.e.*, function vicariously.

Modern experimental evidence, however, points more and more in the direction of a second possible answer, *viz.*, *equipotentiality* of a system. This term means that the parts, and only the parts, remaining in a system may take over functions of that system. We have already seen this principle illustrated in the case of paralysis and the motor system (Chap. XV). Lashley and others who have carefully examined the clinical evidence believe that this principle also explains recovery of memory. They conclude that there can be recovery of memories only so long as parts of the system normally used or available for use in a memory are left intact. Other parts of the brain outside the particular system cannot function vicariously. Without arguing the details of the clinical evidence, let us for the present accept this conclusion until there is good reason to think otherwise.

Mass and Recovery. Adding support to the conclusion and providing another important point about recovery is the fact that recovery of function depends upon the mass (or amount) of the regions of the cortex that are involved in a memory and that are left uninjured. A good illustration of this point is supplied by Lashley. In reviewing the literature on aphasia, he brought together 18 cases of individuals who had lesions in the left third frontal convolution. As we shall see in more detail below, this has been regarded as the "speech area" in man. Lashley ranked these patients for the amount of this area that was damaged by the lesion. He also ranked them for the degree to which they later recovered from the aphasias produced by their lesions. The correlation between these two rankings was .90. Interpreted, this correlation indicates that the more of the "speech area" a patient had left, the more he recovered his ability to use speech. The mass of the cortical area remaining was therefore a crucial factor in recovery.

THE FACTOR OF AGE

When we think about both habits and the organs of the body we recognize that young people are more 'flexible' than older ones. Young organisms can certainly recover from injury and illness more quickly. Do they, however, recover better from brain lesions? Or do they suffer as much impairment as older people? These questions fall under the general heading of equivalence of structure, and we will now take them up briefly.

Basic Functions. It turns out that we must distinguish between simple and more complex functions. In the simple sensory-motor capacities and learning capacities, a brain lesion in infancy does less harm than it does in an adult.

This is seen in comparing the motor capacities and the motor skills of persons injured in infancy and in adulthood. Those with the lesion in infancy do better. This point has been tested in animals with the same result. Rats with some 40 per cent of their cortex taken out in infancy have practically no impairment in learning a maze, whereas the same amount of injury in the adult causes much more deficit in rate of learning (Tsang). Results of this sort have even been shown in form discrimination. Destroying the striate cortex in the adult rat destroys the capacity for form discrimination, but the same operation in infancy leaves some animals with some residual pattern vision (Tsang).

What this means, of course, is that animals and people recover their *basic* sensory, motor, and learning capacities to a greater extent when injured in infancy than when injured as adults. Why that is the case is something we are not sure about. One guess is that parts of the nervous system injured in the infant may regenerate in time. This is a bad guess, however, for such regeneration has never been found when people have looked for it. Other possibilities are better, but they are rather vague. Lashley puts them this way:

> It may be that there is normally a regression of the capacities of lower centers during development and that this regression is prevented by the destruction of higher centers. Or it may be that long continued training can restore not only specific habits but also can build up more general capacities.[1]

Complex Memories and Abilities. Complex functions such as language and general intelligence tell a different story, as Hebb has well shown. He ran a number of tests upon patients with adult and infant injuries. Among his tests was a standard test of intelligence, the Stanford-Binet, which deals with many aspects of memory and mental performance but which can be broken down roughly into verbal and nonverbal items. He tested one group of individuals between ten and nineteen years of age who had suffered brain injuries in infancy. They showed impairment of both verbal and nonverbal functions. In general, however, their verbal capacity was affected most. On the other hand, it was remarkable that individuals who got their brain lesions as adults had no impairment on the verbal items of the intelligence test but were rather impaired on nonverbal capacities. Hebb considered carefully where the brain injuries were in his two groups and has given us convincing evidence that the places of injury do not account for the differences between them.

We need, then, a concept for understanding why infant injury causes impairment in both verbal and nonverbal functions while adult injury impairs nonverbal functions the most. The hypothesis that comes to mind is that the hemispheres and different areas of the cortex are more interdependent in *learning* habits than they are in the memory of the habits once they have been acquired. More specifically, nonverbal habits are instrumental in the development of verbal memories, but once acquired, the verbal functions are not affected by injuries that affect the nonverbal functions. That is what Hebb says in a somewhat different way: Two factors are at work in psychological performance, one being "present intellectual power, of the kind essential to normal intellectual development; the other being the lasting changes in perceptual organization and behavior induced by the first factor during the period of development" (Hebb, page 287).

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[1] P. 751.

BEHAVIOR DISORDERS IN BRAIN LESIONS

We are now about ready to take up particular types of behavior disorder and the question of how they depend upon different types of lesions in the brain. We shall do this in two stages. In this section we describe and classify the ways in which behavior can and does change in brain injury. In the last section, following this one, we shall consider the problem of localization of memory functions.

Clinical neurologists have a long list of names that they apply to losses of memory and other kinds of losses occurring in brain injury. We shall come to some of these names a little later, but for the moment it is better to ignore them and to use some common sense. When we do that we see that there are several possible levels of impairment. The lowest is the loss of sensory and motor capacities, and the highest is the loss of linguistic and symbolic functions. We shall take up briefly each of these levels in turn.

Sensory and Motor Capacities. Obviously, the first link in behavior is sensory capacity. Can we see, hear, and feel? We may have these capacities without ever having learned anything. If we do not have them it matters little what we have learned, for we cannot react to the appropriate stimuli. So we must recognize blindness, deafness, and anesthesia as disorders of sensory capacity, which may occur along with memory disorders but should not be confused with them. We know, too, that different aspects of sensory capacity depend upon different parts of the nervous system, and so we can expect some kinds of sensory capacity to be impaired without damage to other kinds.

At this same level is the paralysis that can occur with injury to the pyramidal system. Without being able to make movements, we cannot learn very much, and even if we have learned a lot we cannot show it very well unless we are able to move. So motor deficits, like sensory deficits, can occur either with or without disorders of memory, but they should not be confused with the latter.

Recognition and Skilled Acts. Above the level of sensory capacity and at the first level of memory is the recognition of the meaning of objects. If we see a banana we know that it is for eating. Or we know that doors are for opening and walking through. Bolts are to screw things together. Or more generally we learn what to do, or what we can do, when any particular stimulus is presented to us. The simplest case of recognition of objects occurs in conditioning an animal to respond to a signal or to choose one of two stimuli to get food. Even this kind of memory can, of course, get rather complicated in man.

When recognition is lost in brain lesions it is called *agnosia*. We can have all sorts of agnosia. The main classes are obvious: visual agnosia, auditory agnosia, and tactile agnosia. Theoretically there are gustatory and olfactory agnosias, but whether they happen in practice is debatable. There may, moreover, be rather specific agnosias within a particular modality, *e.g.*, color agnosia, finger agnosia, form agnosia, and so on. Clinical neurologists have made up names to cover each of the many possible agnosias. With a little Latin, some common sense, and knowing what an agnosia is, you can usually figure them out.

At the same level as recognition but on the motor side of things is memory for acts and skills. These are matters of putting together particular movements into a pattern that accomplishes something. A rat or cat put into a latch box must learn, for example, to go to one end of the box, pull a string, and push a door with its head. Thus it learns to put its basic motor abilities to use to get food.

People with brain lesions can forget skills or acts of this sort without becoming paralyzed or losing their basic motor capacity. When they do they are said to suffer from *apraxia*, which means "inability to do things." The apraxic person may, for example, not remember how to do what he has been doing all his life, like buttoning his shirt, driving a car, opening the door, eating with knife and fork, and so on. There are different descriptions and names for these different apraxias. The important point to note, however, is that people may forget how to carry out acts without suffering any paralysis of movement.

Reminiscence, Recall, and Imagination. So far we have distinguished two levels of function, one of them the primary level of sensory-motor capacity and the second one memory for the meaning of objects and for skilled behavior. In the psychology of learning, however, there is another distinction which can serve us well here. It is the difference between *recognition* and *recall*. In general the clinical neurologists have not made this distinction in dealing with brain lesions, but one of the most recent students of the field has (Nielson). He suggests that we use the word *reminiscence* for this higher level memory and that we speak of its disruption as *irreminiscence*.

The name is not especially important, but the idea is. The idea is that, in addition to recognizing objects and carrying out skills, we also imagine or 'relive' various sensory and motor experiences. As the old English associationists would say, we have "images" or "ideas." In the mental (brain) processes that go on between some stimulus and some response, we may arouse an "image" or memory of an earlier stimulus or experience. Psychologists in general pay little attention to this possibility, and some would deny it entirely. It is, however, a logical possibility, and Nielson, one of the modern authorities in clinical neurology, believes we need it to understand the disorders occurring in brain lesions. Patients, he holds, sometimes have their primary loss in the functions of images and recall rather than in simple agnosias and apraxias.

Language Disorders. The last level of memory to consider in this connection is that of language. By the term "language," we mean all symbolic stimuli and responses that are learned and used by both people and animals—mainly people. Various sorts of signals and gestures fall within the scope of the term. So does arithmetic, algebra, and higher mathematics. Any item of behavior may be called linguistic behavior if it is a symbol for some other behavior. And any stimulus may be called linguistic if it stands for some other stimulus. It is the symbolism that makes language a higher order memory function.

Language, of course, has its own levels of complexity. There are alphabets to learn, words must be spelled, names must be learned, words must be put together in sentences. We may merely recognize the meaning of words and sentences or we may also recall the names of objects and be able to construct words and sentences. Thus linguistic behavior has all the aspects of any other kind of behavior. It is simply a kind of behavior in which man has specialized and which makes up an amazingly large part of his memories as well as his repertoire of adjustments to the world.

Any disorder of language that results from brain injury or disease is called *aphasia*. Obviously, we may have, and do find, both sensory aphasias and motor aphasias in patients, and we have names for all the varieties we run into. Some cannot understand printed language; they have *alexia*. Some cannot understand spoken language; they have word deafness. On the motor side are many shades and varieties of motor aphasia. Sometimes people just cannot form and say words, and this defect is called *verbal aphasia*. Sometimes they cannot name objects correctly; this is *nominal aphasia*. There is no need to go into all the problems of terminology (see Weisenburg and McBride). Some of the chief terms and distinctions are given in Table 7.

The Relation between Levels. Physicians know that naming a symptom is not diagnosing a disease, but they often find it hard to tell just what is a symptom and what is a fundamental part of a disease. So it is with memory disorders. By careful examination we may be able to tell what sorts of disability occur in a patient. It may not always be clear, however, how the disabilities are related and particularly which ones are primary and which are secondary.

A patient, for example, may have a verbal aphasia—he may not be able to speak words or sentences. He may have his 'mind' full of things to say and he may know what he wants to say, but he may simply be unable to say it. He may prove that to you by writing everything perfectly well. If that is the case, the patient has a true motor aphasia. On the other hand, he may say nothing because he has nothing to say. He may have lost his ability to read, to understand what he hears, to recognize the meaning of objects—he may have a widespread agnosia and sensory aphasia—and thus it may be a sensory rather than a motor disorder that keeps him from talking. By ingenious methods of testing and study it is possible to separate different kinds of disorder, but it is very easy to confuse them, because so often one disorder may depend upon another. Table 7 contains an outline of the kinds of memory disorders.

TABLE 7. A BRIEF OUTLINE OF MEMORY DISORDERS *

Sensory Aphasia
- *Auditory aphasia* (*word deafness*): difficulty in understanding the meaning of words and language as heard.
- *Visual aphasia* (*word blindness, alexia*): disturbances of the perception of the meaning of language as read.

Motor Aphasia
- *Manual aphasia* (*agraphia*): difficulty in writing language.
- *Speech aphasia* (*word muteness*): inability to express language vocally or to think in terms of it. Head distinguishes four types of speech aphasia:
  - *Verbal:* "defective power of forming words, whether for external or internal use."
  - *Syntactical:* "lack of that perfect balance and rhythm necessary to make the sounds uttered easily comprehensible." Articles and prepositions binding words together tend to be dropped or slurred.
  - *Nominal:* inability to use words as names and failure to appreciate the nominal character of words.
  - *Semantic:* disturbances of the connected sequence of verbal or written expression.

Agnosia: disturbances in the perception of the significance of sensory stimuli or defects of imagination.
- *Astereognosis:* "difficulty in the recognition of objects or forms by touch."
- *Auditory agnosia:* "psychic deafness for noises and music deafness" (sensory amusia).
- *Visual agnosia:* disorders of visual recognition of
  1. Objects or pictures.
  2. Color—not color blindness or color defect but "difficulty in understanding colors as qualities of objects, a faulty color concept, and an inability to evoke color images."
  3. Visual cues orienting the person in space.

Apraxia: disturbances of the memory of movements.
- *Limbkinetic:* the patient "appreciates the nature of the movement but cannot carry it out with ordinary skill." It is thought to be a loss of innervatory memories for complex forms of movement.
- *Ideokinetic:* a disorder attributed to a break between the kinesthetic processes and others of the brain; consists of loss of memory of how to make movements.
- *Ideational:* faulty conception of the movement as a whole. The patient, for example, is unable to strike a match.
- *Constructive:* "In typical cases the patient experiences difficulty in laying out sticks to copy a given design, in building with blocks, in drawing," and so on.

* Adapted from Weisenburg and McBride.

THE LOCALIZATION OF MEMORY FUNCTIONS

From the rough analysis of levels of memory that we have just given, we can go on to take up the question of how different memory losses depend upon different aspects of the brain's function. This is a question that has provoked much disagreement. On one side are those who believe in strict localization of functions (Henschen; Kleist) and on the other are some who believe in very little localization (Goldstein). In between are some moderates who see memories as depending on many areas but on certain areas more than others (Jackson, Head).

We cannot slip around the disagreements and still say very much about the problem. What seems best is deliberately to take a bias in favor of localization of functions. In that way we can present what is probably the consensus of opinion of the majority of clinical neurologists. We can also present some hypotheses about brain functions which have not yet been tested and which may prove fruitful in the future.

THE CORTICAL AREAS

As we have already seen, there are many ways of naming cortical areas. Brodmann's system, based on architectonic structure, gives us a set of numbers. We also have anatomical names taken from the position of different areas. Occasionally we have run into names, like striate area, that come from some special characteristic of an area. Now, finally, we may consider another set of names for many of these areas—names that are intended to indicate the functions of these areas in memory.

Area for Visual Recognition. This has long been considered to be the parastriate area, or area 18 of Brodmann, which lies next to the primary striate area (see Fig. 163). When it is injured, visual agnosias frequently result (Nielson). Some believe that one side of the parastriate cortex becomes major and the other minor relatively early in life, but the degree of dominance is not very great. It may be greater in some individuals than in others. Thus removing the minor area usually has very little effect, but removing the major area has considerable effect, from which the individual usually will recover without too much retraining. The major side is usually, but not always, the same as the major side for language and handedness.

Area for Visual Reminiscence. This area has been emphasized more by Nielson than by the older, classical neurologists. It is considered to be the peristriate area (Brodmann's area 19), which lies next to the parastriate area (see Fig. 151). This area, according to Nielson, is necessary to enable us to visualize objects we have seen in the past, *i.e.*, for us to have "visual imagination." He believes that the area on one side of the brain is somewhat the major and the other somewhat the minor but that cerebral dominance is not pronounced. If that is the case, we could expect that lesions on the major side of either this area or the area of recognition would produce mild effects from which there might be recovery, but that pronounced disorders would not appear unless the areas were removed on both sides.

Areas for Reading. The angular gyrus, called 39 in Brodmann's system, has often been regarded as the center for reading language, *i.e.*, for understanding the meaning of the symbols appearing on the written or printed page. Just why there should be a special area for this function is not clear. It is true that area 39 seems to be a 'new' area in man, which does not exist in the monkey. Clinical neurologists also can present cases with marked disability in reading (*alexia*) after lesions of this center on the major side. In this case, too, the difference between the major and minor side is considerable. Injury to the minor side ordinarily does practically nothing, whereas injury to the major side may produce practically complete alexia. According to Nielson, the major reading area has a double function. It not only serves in the recognition of printed words but also in their revisualization.

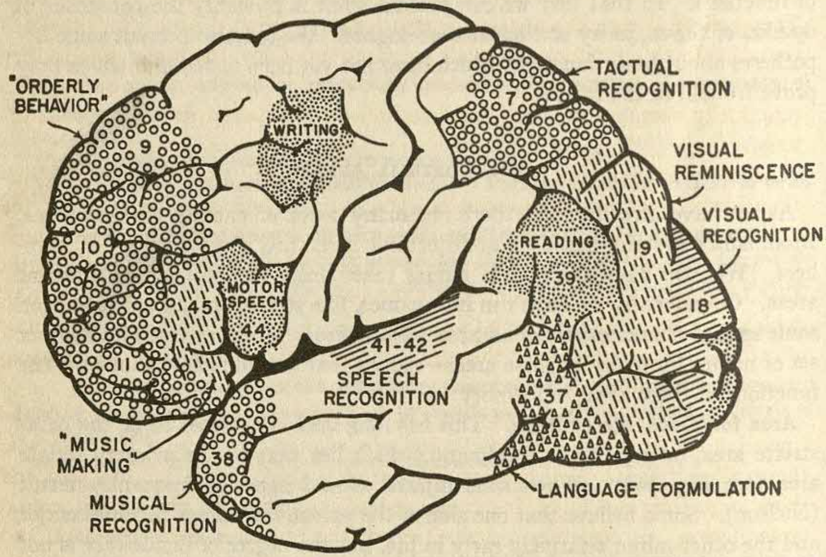

FIG. 163. Composite diagram of the supposed "association" areas of the human cerebral cortex. Many neurologists believe that the cortex functions in some such way as indicated; some do not. The scheme is worth while mainly to provide hypotheses for further research and to help in thinking about the role of the cortex in learning and memory.

Area for Tactile Recognition. The posterior parietal lobule, primarily area 7, has often been considered the tactile "association" area. As such, it presumably is responsible for the recognition of tactile objects. We have pointed out in an earlier chapter, however, that this notion does not fit with recent physiological evidence. This would lead us to believe that the tactile association area lies laterally, rather than dorsally, on the parietal lobe. In fact, unless the areas have been drastically rearranged in the evolution of man, the tactile "association" area might better be put where area 40, the supramarginal gyrus, appears on the diagram of Fig. 163. It could turn out, indeed, that area 40 is the area for tactile recognition and that area 7 is the area for tactile reminiscence comparable to area 19. It will take a lot of research, however, before we are straightened out on this question.

Areas for Recognizing Speech. In man there are two small areas of the temporal lobe, in and near the lateral fissure, which together are sometimes called *Wernicke's area*. They are concerned with hearing—that we know—but it has not been clear whether they have separate functions or the same function. Neurologists have usually considered that the area is partly concerned with auditory memories and association. Some are even more specific. They believe Wernicke's area is the area for recognizing the meaning of speech sounds. In this function, as in all language functions, the major side is very much superior to the minor side, so that a lesion on the major side causes practically complete loss of ability to understand spoken speech (word deafness).

Area for Recognizing Music. As laymen and as psychologists we can distinguish between music and speech. It is hard to believe, however, that the brain is so organized that it has its memories for speech in one place and those for music in another. Yet many neurologists believe their evidence indicates that. The area assigned the duty of recognizing music is area 38 (see Fig. 163), which makes up the tip of the temporal lobe. There is supposed to be a little dominance of one side over the other but not very much. For that reason, losses of musical memory (amusia) are rather rare.

Area for Writing Language. In Fig. 163 you see an area marked as the "writing center." This is sometimes called *Exner's center* after the man who first called it that. Neurologists differ in just where they place this area and how large they make it. In general it lies in and around the second frontal convolution. It certainly includes part of the premotor area—the hand and arm area. Perhaps it also includes part of area 9 of the prefrontal areas. We have already seen that the premotor areas have something to do with the "synthesis" of movements into acts (Chap. XV). Perhaps it is reasonable, then, that a lesion in this general region would interfere with the memory and fine skill of writing language.

Area for Speaking. Below the writing area in the third frontal convolution of the frontal lobe is the area that appears most important in our ability to talk. This is the best known of the areas involved in aphasia, having been described first by Broca in 1861. Anatomists are not sure just how it is related to the rest of the frontal lobe (see Bucy). It lies at the foot of area 4 (the motor area) and area 6 (the premotor area), as well as the forward prefrontal areas, and is given the number 44. It is certainly part of the general facial subdivision of the frontal lobe. It seems, however, to have been specially differentiated to be a center for coordinating speech. Moreover, one side 'dominates' the other side to a considerable degree, so that injury to the major side can cause an almost complete motor aphasia while a lesion on the minor side may have no detectable consequences.

Area for Making Music. With some skepticism we must next point out that an area called area 45, lying just in front of Broca's area, is supposed to be important in singing and playing instruments (Nielson). It seems a little hard to believe that there should be a special center for such activity, yet there may be a little sense to it. "Making music" is a rather complex skill of making acts quickly in the correct sequence. Perhaps, therefore, the part of the prefrontal areas in the facial subdivision most connected with speech and the mouth is more involved in music than other areas.

Areas for Orderly Behavior. We do not fully understand the functions of the prefrontal areas, and what we do know we have no simple name for. They have something to do with attention, we know that, and perhaps that is the important aspect of their function. However that may be, it is characteristic of prefrontal animals that they forget the order in which to do things. Although they may know what to do, they do not know what to do next and how to do each thing in the correct order. So it is in human brain lesions. We often see disturbances of orderliness of behavior and loss of memory for the order of acts in cases of prefrontal lesion (Freeman and Watts).

Area for Formulation of Language. An idea that is new with Nielson and relatively recent is the notion of a special area for formulating language. By this he means a center for tying together the activities of the other language centers in the angular gyrus, Wernicke's area, and Broca's area. To formulate words we sometimes have to visualize them, or imagine hearing them, or even try saying them to ourselves. All these activities may be going on in trying to find our words and formulate sentences, whether written or spoken. Nielson believes that one area, area 37 in the temporal lobe, coordinates these activities. He believes, too, that the major side is rather important, that without it there is great disturbance of language formulation, but that in the course of time the minor side can take over the function.

Conclusions. It is hard to tell how much truth there is in these ideas of localization of functions in different areas of the cortex. We can be sure that they are not entirely correct. Yet we cannot wholly reject them. For the time being, whether we accept them or not, we probably should consider them as hypotheses to keep in mind in interpreting further clinical studies and in planning research programs in animals.

THE EFFECTS OF BRAIN LESIONS

Even if the wildest ideas of localization of memory functions were correct, we would expect not to find localization too obvious in clinical cases of brain lesion. In the first place, where there is not complete dominance of one hemisphere we seldom will see lesions so placed that they damage the same areas on both sides. Secondly, there may also be rather large individual differences in the degree to which one side is major and the other minor. Finally, and most important, impairment of different memory functions through lesions in different areas may very often produce superficially similar behavior disorders. A patient with a lesion, for example, that makes him unable to understand spoken words usually does not talk very much. He may seem to have the same loss of speech as another patient with a brain lesion that makes him unable to formulate words or sentences even though he can understand speech. The causes of 'speechlessness' in the two cases may be quite different and the lesions may be quite different, but superficially the two patients may seem to have the same trouble.

With these thoughts in mind let us take up now some of the results of studies of cases with brain lesions. Although there are hundreds of such cases, we should rely most on the study of Weisenburg and McBride. It is the most recent carefully reported study, and it is reasonably conservative in its conclusions.

Receptive Disorders of Memory. Receptive agnosias and aphasias are seldom seen in pure form in cases of brain lesion. What may seem to be a pure, isolated aphasia fails to hold up under careful psychological examination. Pure word blindness and pure word deafness probably do not exist. If there is one type of disorder present, the other kind is usually present too in some degree. One type of disorder, however, may be much more serious than the other, and one may be much more prominent than the other. This is entirely reasonable, for as we have already emphasized, our different abilities and memories certainly depend upon one another.

There is a considerable degree of functional localization of receptive disorders. Take two cases as examples whose lesions were known well and whose psychological examination was rather complete. In one case the lesion was in the occipital area (German and Fox). Visual recognition was greatly disturbed. The patient could not name an orange by looking at it, although she could when she smelled it. Yet she did not have much trouble with auditory recognition, for she could recognize the ringing of a bell even when she could not tell it by looking at it. In a second case there was damage to the temporal lobe (Fox and German). The memory disorders were in listening to speech and in recognizing sounds. The patient could not understand spoken commands, although he could read them when written. So there was a fairly clear auditory agnosia and aphasia without much visual involvement.

This is not the whole story. When much more complex functions are studied, there turns out to be less localization of function. In the last case, for example, the patient had a lesion of the temporal lobe and had much more auditory agnosia than visual agnosia. He nevertheless did have trouble both in listening to and reading words. The difficulty became most apparent only after reading for some time, but it was there. Weisenburg and McBride, after looking at a good many cases, also conclude that the more complex aspects of receptive aphasias are not very localized, that where there is a disturbance in one sphere there usually is one in the other.

Expressive Disorders of Memory. Similar conclusions apply to the motor, or expressive, functions. Here, too, there is a difference between the simpler and more complex memories. Most neurologists, for example, now accept the distinction between *reactive* and *propositional speech.* Reactive or emotional speech tends to be ejaculatory or automatic, and it represents only some vague feeling of the patient. Examples of this type are "oh! dear me," "yes," and "hello." Propositional speech, on the other hand, represents definite objects or actions, as well as relations between them, imagined by the speaker and guiding his speech. This therefore involves complex processes, including thought and imagination, to a greater degree than reactive speech.

These two aspects of linguistic memory have different physiological bases. Reactive speech depends almost equally on both hemispheres, not on a major hemisphere. A patient can display reactive speech no matter which hemisphere may be injured. On the other hand, propositional speech, which makes up the greater part of speech, depends upon a major hemisphere. In most people this is the left hemisphere. Removing part or even all of the minor hemisphere does practically nothing to such speech, but removing the areas of the major hemisphere abolishes it.

Moreover, propositional speech depends upon particular areas of the major hemisphere. If a patient has such a complete verbal aphasia that he cannot even repeat back what is said to him, he probably has a motor aphasia that can be assigned to Broca's area. If, according to Nielson, a patient can say words but has great trouble formulating them into statements, the lesion is most likely in area 37, his "language formulation area." On the other hand, more restricted aphasias, such as inability to name objects or to recall names, are usually not motor aphasias but types of receptive aphasia that prevent the proper use of speech. The lesions, in that case, are usually in the posterior part of the brain.

Amnesic Aphasia. There is one kind of aphasia that appears in relatively pure form and has been recognized by all workers in the field (Weisenburg and McBride; Head; Harlow). It has had several names, but one name that is used most frequently is *amnesic aphasia.* In this disorder the individual no longer can recall the name of an object, although he may be able to recognize the name as soon as he sees it or hears it. Once he has found it the patient repeats the word or name with satisfaction, but he soon forgets it and a few minutes later he is usually unable to recall the name again without prompting.

Although it is easy to describe, this kind of disorder is probably rather complex. Naming objects may involve some 'visualization,' some 'auditory reminiscence,' some 'talking to oneself,' and perhaps other types of linguistic processes. Most neurologists, at any rate, have considered amnesic aphasia to be a disorder of complex language functions. What makes them think so is the fact that amnesic aphasia is one of the first disorders to appear in brain damage. It may appear when the damage is very mild and when no other language disorders show. Moreover, this kind of aphasia may occur with lesions in almost any part of the major hemisphere—lesions that simply disrupt in some way some part of the system of "speech centers" of the hemisphere. That makes us think that ability to recall is not a simple but rather a complex memory function involving a fair share of the cerebral hemisphere.

Categorical Behavior. There is a somewhat different view of amnesic aphasia from that we have mentioned so far. It is Goldstein's. To him amnesic aphasia is not just inability to recall names. The trouble goes deeper. It is impairment of categorical or abstractive behavior—impairment of ability to recognize an object as a member of a class of objects. A patient, for example, who shows a loss of categorical behavior may not be able to name a "book," although he may recognize what is done with it and prove it by opening and reading the book when it is handed to him. He has apparently lost the ability to name the class of objects of which the particular book is a member. To illustrate further, if told that the book is a book, the patient may thereafter be able to use the name with the particular book to which the symbol has been attached but not to recognize that the name also goes along with other books, *i.e.*, the class of books.

Not every one agrees with Goldstein that categorical or abstractive behavior is the real trouble in amnesic aphasia. Goldstein nevertheless has a good point in emphasizing that abstracting is a process that is sometimes essential in a disturbance of language and that it is easily upset by cortical damage. Goldstein, in fact, has good evidence from his clinical studies that brain lesions first affect abstract behavior and then, as they become more severe and extensive, invade the more primitive "concrete" aspects of behavior of the lower orders.

Nonlinguistic Functions. In coming to the close of this chapter, we ought to say a word about memories not involving language. Such memories are not so dependent upon a major hemisphere as is language. There may be a major and a minor hemisphere, but the difference between them may not be great. Proof of this point comes from a study by Weisenburg and McBride of 22 cases in which lesions were restricted to the right (minor) hemisphere. In none of them was there any aphasia. The subjects were given several tests of arithmetic and nonlinguistic ability. They were then compared with control cases matched with them in respect of age and general history except that they did not suffer from lesions. The investigators found the patients inferior in all performances that they tested, particularly in arithmetic and the learning of a maze problem. The defects of these patients, therefore, were marked in non linguistic functions but insignificant in the area of linguistic memory. From this study Weisenburg and McBride conclude that although linguistic functions are confined primarily to the major hemisphere, nonlinguistic memories are not.

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CHAPTER XXV

BEHAVIOR DISORDERS

What lies behind the major disorders of behavior is a challenging problem for the psychologist. At best the problem is a hard one, but what makes it even harder is the line that is so often drawn between "functional" and "organic" disorders. This is an artificial line, because any function, normal or abnormal, is organic, and any organic change in the brain or its environment usually shows up in function. Moreover, we have been learning more and more in recent years that disorders of behavior often are at the root of physiological disorders —the so-called *psychosomatic* diseases. So, as a practical matter, the physiological and psychological factors in behavior disorders are closely linked together.

Consider such disorders as epilepsy, feeble-mindedness, and the psychoses. We can describe in each case what the behavior is like, and sometimes we account for some of it by knowing what happened in the life history of the patient. However, we must be able to say why some individuals develop disorders, while others, with about the same kind of life, do not. Those who do, we now know, usually have some genetic, chemical, or neural predisposition to react to stress in the environment by developing a disorder of behavior. In other words, both the body and the environment have something to do with the disorder. Here, in a book of this kind, we shall stress the physiological basis of behavior disorders, without intending in the least to deny the roles of learning, experience, and environment.

CONVULSIVE DISORDERS

The epilepsies are most striking disorders of behavior, for people who have them usually also have convulsions. Convulsions are patterns of behavior that may take place in only one part of the body or in the musculature of the entire body. They consist of violent contractions of muscles. Sometimes these contractions come in bursts with relaxations in between, and quite violent movements result. In this case the convulsions are called *clonic*. Sometimes the contractions go on without stopping and the body is held rigid with the muscles 'locked.' Such convulsions are *tonic* convulsions. In any particular convulsive episode one may see either one or both types. Very often tonic seizures come first and then pass gradually into clonic convulsions, or the two may alternate with each other several times. After the convulsions subside, a period of subnormal activity or *coma* usually follows, and in this state the limbs become waxlike and easily molded.

Epilepsy. As you will see, convulsions in both man and animals have many causes. When they occur in humans, we usually take them to be signs of epilepsy. Although the layman thinks of epilepsy as a disease, it is actually a name given to many kinds of disorder, which may have quite different causes. As a matter of fact, not all kinds of epileptics have convulsions. About the only common feature that seems to be the same in the different kinds of epilepsy is a large rhythmic discharge of neurons of the brain, spreading often from one area to another. Apparently neurons in any part of the brain are subject to these discharges. The places where they occur and the distance that they spread often help us to tell different clinical types of epilepsy from one another (Penfield and Erickson; Table 8).

TABLE 8. MAJOR SYMPTOMS CHARACTERISTIC OF DIFFERENT TYPES OF EPILEPSY

Type of Seizure	*Symptoms*
Focal convulsive	Starts in extremity and spreads over body, following pattern of motor points on the cortex; consciousness usually retained
General convulsive	May begin with sensory hallucination, or aura, and loss of consciousness and of upright posture; then tonic-clonic convulsions and coma follow in that order
Petit mal	Brief lapse of consciousness or momentary mental confusion; may involve slight twitching of face muscles
Psychical	Dreamy state with hallucinations, illusions, and feelings of strangeness; vivid memories and compulsive thoughts may occur; awareness of real environment not always lost

Brain Waves and Epilepsy. The discharges of neurons that go on in epileptic attacks show up in records of electrical activity taken from electrodes on the skull (see page 544). In such records we can see typical signs, not only while an individual is having an attack, but also when he is not. In fact, a *dysrhythmia* in the electrical record often reveals epilsepsy before a person has ever had an attack. The normal "brain wave," as we shall see in the next chapter, has a lot of alpha waves of about 10 cycles per second. The brain waves of the epileptic, however, tend to be either faster or slower than this. Sometimes they are both in alternation.

Dysrhythmia is often present in epilsepsy that is due to injury of the brain. Yet dysrhythmia is not necessarily a sign of brain injury. Rather, it seems to stand for some general functional defect of the nervous system, probably having to do with the way all the nerve cells behave. Supporting this view is the fact that cerebral dysrhythmia is inherited and along with it is a predisposition to epileptic attacks (Lennox). Dysrhythmia occurs much more often in close relatives of epileptics, for example, than it does in the normal population. In the case of twins, furthermore, the twin of an epileptic patient almost always has dysrhythmia whether or not he is epileptic. Dysrhythmia, however, is not a sure sign of epilepsy, because almost 10 per cent of the population have it while only 0.5 per cent of the population are epileptics. But it is helpful in diagnosing epilepsy, because it occurs about thirty times as often in epileptics as in normal people.

EXPERIMENTAL SEIZURES

We have been learning a lot about epilepsy in recent years by causing convulsions experimentally in animals. There are three principal ways of doing that: electrically, chemically, and acoustically. We shall take each of them in turn.

Electrical Stimulation. As noted in an earlier chapter (Chap. XIII), we can make some part of the body move by applying a weak current to a point on the motor cortex. If the stimulus is applied for a long time, however, or if it is quite intense, there will be a localized convulsion in the part of the body affected, which may spread to involve most of the musculature (see Fulton). With very strong stimulation, it does not matter where the electrodes are placed. Neural activity develops in the whole cortex and expresses itself as a generalized tonic-clonic convulsion. We can bring about the same type of convulsions by applying alternating current to the skull rather than directly to the brain, but naturally the strength of the electrical stimulus must be much greater in this case. Again, if the current is relatively weak, the seizure may be weak or incomplete. In fact, relatively weak electrical stimulation in rats brings out a running attack rather than a full tonic-clonic convulsion (Golub and Morgan).

Chemical Agents. We can also bring about experimental seizures by *chemical means* such as drugs and poisons. One of the interesting things about the chemicals that induce seizures is that they act at different levels of the nervous system. Thus we know that convulsions can start in almost any part of the nervous system (Penfield and Erickson). Some drugs like veratrine or eserine can directly affect the muscles or efferent nerves, thereby causing convulsive attacks. Others may have an effect on the spinal cord (strychnine) or medulla (picrotoxin). Still others, like metrazol, mainly affect the cerebrum.

The convulsive drugs serve to tell us about the susceptibility of people and animals to different types of seizures. Epileptics are more susceptible to convulsive drugs, for example, than normal people. Similarly, subconvulsive doses of drugs like metrazol make animals more susceptible to seizures brought about by other means such as electrical or auditory stimulation (see below). From these studies we can see that chemical changes may sometimes have their part in causing convulsions, both epileptic or experimental. We can reach that conclusion, too, from other facts that we shall come to in a moment.

Audiogenic Seizures. A third type of experimental convulsion that we see in some animals is the *audiogenic seizure.* Some cases of human epilepsy have been reported in which attacks apparently are brought on by auditory stimulation, particularly by music. Similarly, sound-induced seizures occur in the dog, cat, guinea pig, and mouse, but most of the experimental work has been done on the rat. All that is necessary to bring on audiogenic seizures in susceptible rats is to stimulate them with a loud sound—a sound that is loud for the rat—for several seconds (Morgan and Galambos). The attack then begins with wild, heedless running. It may end up sometimes, but not always, in violent tonic-clonic convulsions and coma.

Many factors aside from the intensity of the stimulating sound have something to do with audiogenic seizures (see Finger). We shall take up some of these factors in a moment when we consider the physiological basis of convulsive disorders, but we can mention a few here. For one thing, the age of the animal is an important factor in audiogenic seizures. Susceptibility to seizures increases up to about one hundred and thirty days of age and thereafter declines. As you will see later, furthermore, the nutritional status of the animal makes a great deal of difference in its susceptibility to audiogenic attacks. In fact, simply taking food or water from animals for 24 hr. increases the number of audiogenic seizures (Finger). It is clear, finally, that strains of rats differ a great deal in susceptibility to audiogenic attacks. Some strains of rats hardly ever give seizures (wild Norway and Alexandrine rats). In other strains, as many as 95 per cent of animals may have seizures (domesticated gray Norway rats). Most strains, however, yield fewer than 50 per cent susceptible animals.

The fact that strains of rats differ in susceptibility suggests that heredity may have something to do with audiogenic seizures. Supporting this view is the fact that highly susceptible and only slightly susceptible strains of rats may be produced by selective breeding for about six generations (Griffiths). Unfortunately, most strains of rats are not pure enough for good genetic studies, and consequently we have conflicting reports about genetic mechanisms in the transmission of susceptibility to audiogenic seizures. Recently, however, two highly inbred strains of mice have been found which react quite differently to auditory stimulation (Hall). One strain, C57, almost never displays seizures, while most of the animals of the other strain, dba, have violent seizures which usually end in death. By careful crossing and backcrossing procedures, investigators find that the primary genetic factor in audiogenic seizures of the mouse is a single dominant gene, although there may be one or more other modifying factors (Witt and Hall).

NEURAL BASIS OF CONVULSIONS

Although we have many studies of epileptic behavior, unfortunately we have very few direct attempts to study the role of the nervous system in convulsive disorders. There are, of course, a large number of clinical studies of organic epilepsy. These show that convulsions may be eliminated when irritating tumors or scars are removed from various parts of the brain. Unfortunately, these studies do not tell us any more than that seizures may be started by a disturbance in almost any part of the brain. For more specific information we have to turn to the study of the nervous system in experimentally induced seizures in animals. In one experiment on cats, for example, the investigators got full-blown convulsions without the cerebral cortex (Wikler and Frank). They used electrical stimulation to trip off the convulsions, and it turned out that decorticate animals are, if anything, more susceptible to seizures than normal animals. Recordings of brain waves in these cats during the attacks, furthermore, showed the same kind of disruption of electrical activity that can be seen in intact animals having seizures.

Much the same story comes from a study by Beach and Weaver of audiogenic seizures in the rat. Three of their most highly susceptible animals showed an increase in the frequency and the severity of attacks after almost complete decortication. On the other hand, using large numbers of rats of varying degrees of susceptibility, Weiner and Morgan report that audiogenic attacks are lessened by relatively small lesions in the auditory, motor, and frontal areas of the cortex. There is no way to clear up this disagreement in findings at the present time. It is interesting, however, that the rats that did have seizures after removal of the motor cortex in the study of Weiner and Morgan had much longer and more severe attacks than are usually seen. It is possible that the motor cortex normally inhibits the lower centers in respect of audiogenic seizures. If that is so, Beach and Weaver may have gotten their results because they invaded the motor cortex so extensively, but much more research will have to be done before we can understand the neural basis of convulsive behavior.

Chemical Basis of Convulsions

Besides the electrical, auditory, and mechanical causes of convulsive disorders, there can be no doubt that chemical changes in the internal environment can increase the excitability of nerve cells rapidly and set them into rhythmic epileptic discharges. We know, for example, that an increase in the pH of the blood (increased alkalinity) or a brief decrease in the amount of oxygen available makes nerve cells hyperexcitable. In fact, either one of these conditions creates cerebral dysrhythmia and is likely to produce convulsions, particularly in epileptics. Some epileptics, for instance, have convulsions if they hold their breath (hypoventilation) for a short period, thereby depriving the brain of oxygen. More often, convulsions follow hyperventilation (overbreathing), in which carbon dioxide leaves the blood and is exhaled, thereby raising the pH of the blood and increasing the excitability of the brain. Conversely, increasing the acidity of the blood often cuts down the number of seizures in many kinds of epilepsy; *e.g.*, seizures may be alleviated or prevented by fasting, eating a ketogenic diet, breathing carbon dioxide, or indulging in strenuous exercise.

Hydrogen-ion Concentration. The role of pH in convulsive disorders is not a simple one, however. Although many *anticonvulsive* drugs seem to act by reducing the pH of the blood, not all agents that lower pH prevent seizures. The action of *convulsive* drugs is even more complicated. Many of these produce their effects through increasing pH, but others clearly cut down pH. Their manner of action, it seems, is through raising the pH of the nerve cells themselves. Although the reason for the rise in cellular pH accompanying a decrease in blood pH is not clear, the fact itself has been demonstrated. In one experiment an animal was injected with a convulsive drug and the pH of the blood and brain cells was separately recorded (Fig. 164). After the drug injection the pH of the brain cells gradually rose, and when it had reached a certain point, the experimenters could see convulsive discharges from the brain (Dusser de Barenne *et al.*). The pH of the cortex subsequently went down to about the same level as that of the blood, and with that the convulsive discharge stopped. In fact, the general excitability of the brain was depressed, just as one might expect from the fact that a low pH causes a depression of the excitability of nerve cells.

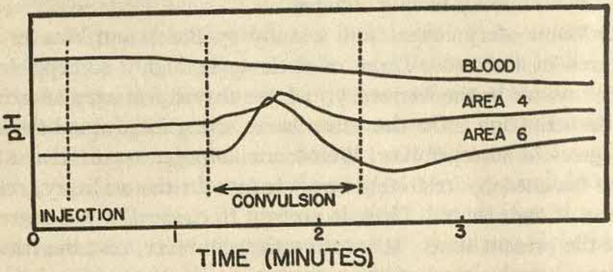

FIG. 164. Changes in the pH of the blood, area 4 and area 6 of the cortex, following the injection of a convulsive drug and accompanying the occurrence of a convulsion. (*After Dusser de Barenne et al.*, 1938.)

Metabolic Factors. Although pH and oxygen may have a lot to do with convulsive behavior, sometimes neither of them is very important. Instead, the convulsions seem to be brought on by the irritating effects of the products of metabolism of nerve cells subjected to oxygen deprivation. In one series of experiments with animals, for example, some physiologists shut off the blood from the head for a few seconds by occluding the carotid arteries (Pollock and Davis). This procedure, of course, caused a cerebral anoxemia and might itself be expected to produce convulsions. It was only after the blood was let back into the brain, however, that convulsions occurred. The experimenters could show, furthermore, that convulsions were set off primarily by materials that had been deposited in the brain during the period of anoxemia. For when they washed out the brain with physiological salt solution during anoxemia, restoring the cerebral blood supply did not produce convulsions. They concluded, therefore, that the acid metabolites of brain activity in the absence of oxygen were the irritating factors leading to convulsions.

Dietary Deficiencies. Somewhat similar to this result are the convulsive tendencies that show up in *thiamin deficiency*. Animals severely deprived of this vitamin can be set into convulsions by almost any rather strong stimulus. Rats that have convulsions when stimulated with loud sounds, for example, are made to have them much more easily and more often when deprived of thiamin (Patton *et al.*). On the other hand, feeding thiamin to rats cuts down their susceptibility to having seizures induced by sound (Patton *et al.*). Thiamin, as you know, is essential in the metabolism of carbohydrate, which is so important for normal nerve function. In its absence, pyruvic acid piles up in abnormal amounts in the blood, and this in itself may contribute to the excitability of cortical nerve cells.

Somewhat different results turn up in *pyridoxine deficiency* (Patton *et al.*). While deficiency of this vitamin encourages seizures, adding it to the stock diet did not prevent susceptible rats from having audiogenic attacks. This is not an unexpected finding, however, for adding pyridoxine to a normal diet probably does not benefit the rat. Yet its absence from the diet will cause anemia, which we know is conducive to nerve hyperexcitability. Adding thiamin, on the other hand, might be expected to prevent seizures, since extra amounts of it can be used in the rapid metabolism of pyruvic acid.

Perhaps an even more interesting finding is the fact that *magnesium deficiency* can lead to "spontaneous" convulsions in rats in the absence of any known auditory stimulation (Patton *et al.*). After just a few days of magnesium deficiency, rats begin to show marked peripheral vasodilation and hyperexcitability. Then, in succeeding days, they show more and more violent running attacks and finally tonic-clonic convulsions. After a few such seizures, many of the animals die in the comatose stage of the attack. Either reduced vitamin B complex intake or high calcium diet aggravates these seizures, but they may be alleviated, for some unknown reason, by simply restricting the intake of pyridoxine. Feeding magnesium will alleviate and eliminate seizures, furthermore, but only if it is administered before the deficiency goes on very long. As you might expect, magnesium-deficient animals are more susceptible to sound-induced seizures than normal animals. This has been found in the case of both the rat and the hamster (Patton *et al.;* Patton). We know, furthermore, that wild Norway and Alexandrine rats, which are not normally susceptible to audiogenic attacks, can be given convulsions if they are magnesium-deficient (Griffiths).

CONVULSIONS AND MEMORY

A little later in the chapter we shall consider disorders of intelligence in some detail. Before we get to that subject, however, we have a topic that is a sort of bridge between epileptic disorders on the one hand and disorders of intelligence and personality on the other. This is the problem of how repeated convulsions affect learning and intelligence.

Epileptic Convulsions in Man. Contrary to common belief, general intelligence is not adversely affected by epileptic seizures (Lennox). Some epileptics, it is true, are also mentally defective, but that may be the result of the same deficiencies of the nervous system that cause the epilepsy itself. The outcome of convulsive shock therapy with human patients, on the other hand, suggests that convulsions can affect certain aspects of intellectual capacity. As you will see, this evidence is supported to a large degree by similar studies of the learning ability of animals.

Therapeutic Convulsions in Man. We know very little of how convulsive therapy affects intellectual processes, despite the fact that it has been widely used in the treatment of many types of psychosis. In most of the cases that have been studied, measurements of intelligence say only that repeated convulsions slightly impair intelligence. So far, the only major effects appear on those parts of the intelligence tests which require the use of memory (Stone). Further investigation into the way in which convulsive therapy affects memory makes us believe that the impairment is primarily a loss of recent memory. In one study where electroshock therapy was used, for example, memory for more recently learned verbal material was much more severely impaired than memory for similar material learned at an earlier date (Zubin and Barrera). Similarly, in the case of metrazol convulsions, patients revert to the older of two simple motor habits which they were taught before the shock treatment (Rodnick). Much more work needs to be done before we can know whether other kinds of human intellectual capacity are also affected by convulsive therapy. At the present time, most of our information comes from the study of learning and memory in animals.

Experimental Convulsions and Animal Learning. Almost all the work on the effects of experimentally induced convulsions on learning has been done on the rat. In some of the earlier studies, no effect of convulsions on learning could be found when either metrazol or electroshock convulsions were used (Bunch and Mueller; Siegel). In these experiments, however, either the convulsions were few in number or else the learning task used was very simple. Later experiments show quite definitely that impairment of learning is clear-cut only when difficult tasks are used (Russell). Even with fairly complex mazes, however, a series of about ten daily electroshock convulsions produces only a slight impairment of learning. This effect shows up when rats are shocked right after weaning and tested anywhere from 10 to 90 days later (Eriksen *et al.;* Porter *et al.*). Similar results have also been obtained with older rats, in whom the effects last at least 30 days (Braun *et al.*). Finally, a slight impairment of learning has also been reported in the case of shock induced by heavy doses of insulin (Riess and Berman).

In all these experiments the convulsive treatment preceded the learning tests. As you might expect, even greater impairments of learning come about when the convulsions are induced every day of learning (Hayes). In such experiments, however, much of the impairment may be due to the fact that the convulsions disrupt memory and prevent the animals from carrying over what they learn from one trial to another. That this is probably the case is strongly suggested by some experiments by Duncan. He allowed rats one learning trial a day in a simple avoidance situation and then subjected them to an electroshock convulsion at varying intervals after the completion of each trial. If he

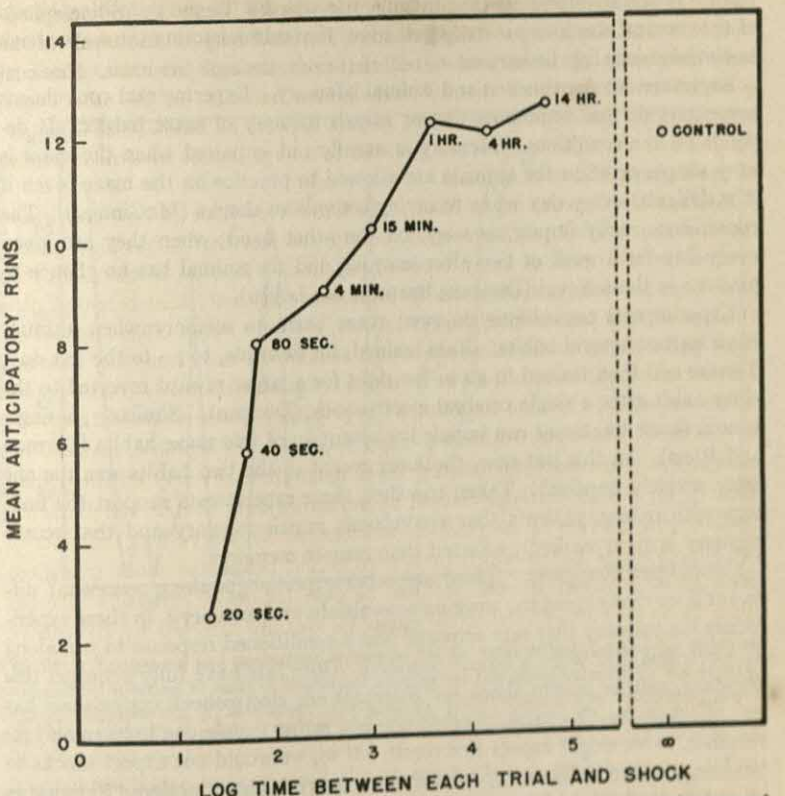

FIG. 165. Degree of learning of a control group and eight different experimental groups of rats given cerebral electroshocks at different intervals of time after each training trial. Learning is expressed as the average number of times rats ran from an electrified grid in time to avoid shock (mean anticipatory runs). (*From C. P. Duncan. The retroactive effect of electroshock on learning, p. 35. J. comp. physiol. Psychol.*, 1949, 42, 32–44. *By permission of the publishers.*)

waited up to an hour after each trial before giving the shock he found that there was little or no effect on learning. If the shock came within 15 min. after the trial, however, the effect was so great that very little learning took place (Fig. 165). That the impairment of learning was not due to the punishing effects of the cerebral shock was shown by the fact that administering the same shock to the hind legs had little effect.

Experimental Convulsions and Animal Memory. Experimental convulsions sometimes do and sometimes do not impair memory of maze habits. It depends on the conditions. Memory is usually not impaired when the maze is very simple or when the animals are allowed to practice on the maze (even if it is difficult) every day while receiving convulsive shocks (McGinnies). The convulsions really impair memory, on the other hand, when they are given every day for a week or two after learning and the animal has no chance to practice in the interval (Duncan; Braun *et al.;* Loken).

Experimental convulsions do even more harm to memory when animals have learned several habits. Rats trained, for example, to go to the left on a T maze and then trained to go to the right for a larger reward reverted to the older habit after a single cerebral electroshock (Duncan). Similarly, a single insulin shock treatment can impair the retention of two maze habits (Berman and Riess). In this last case, the more recent of the two habits was the one more severely impaired. Taken together, these experiments support the findings with human patients that convulsions impair memory and that recent memory is more markedly affected than remote memory.

Conditioned Responses. There are other experiments along somewhat different lines that extend the work on convulsions and memory. In these experiments the memory that rats acquired was a conditioned response to run along an electrified grill when a buzzer sounded. Once rats have fully acquired this response, neither insulin shock nor metrazol nor electroshock convulsions has any effect on it. Of course, the response is a rather simple one to learn and remember, so we might expect this result. If so, we would not expect shocks to have any marked effect on spontaneous recovery from extinction. Yet that is what happens. Convulsions given to animals after their running responses are fully extinguished (by leaving out shock on the grill) bring conditioned responses back to 60 to 100 per cent, yet animals without convulsions make no such recovery (Kessler and Gellhorn). Continuing the extinction procedure after the electroshocks are all over gradually extinguishes the animals again. We get the same general results with insulin shock as with electroshock, but it takes longer for animals suffering insulin shock to get fully extinguished again after shock than it does for animals getting electroshock (Gellhorn and Minatoya). In fact, they may not extinguish after several months of presenting the conditioned stimulus alone (Fig. 166).

On the surface these results may seem to be different from those of the maze studies. The fact, however, that insulin shock and electroshock convulsions bring back conditioned responses fits in with the notion that shock treatment has its main effect on recent memory. First the animal in the conditioning situation learns to run at the sound of the buzzer, then it learns not to run during extinction trials. This is very much like Duncan's experiment, where the rats first learn to go left on a T maze and then to go right. In both cases the shock treatment weakens the second habit and leaves the older habit the stronger. The difficult thing to understand about the conditioning experiments is why a few insulin shocks prevent extinction from occurring when reinforcement is omitted over such a long period of testing. At present about the only guess we have to go on is Gellhorn's suggestion that insulin shock serves to heighten the activity of the hypothalamus and thereby keep conditioned responses active.

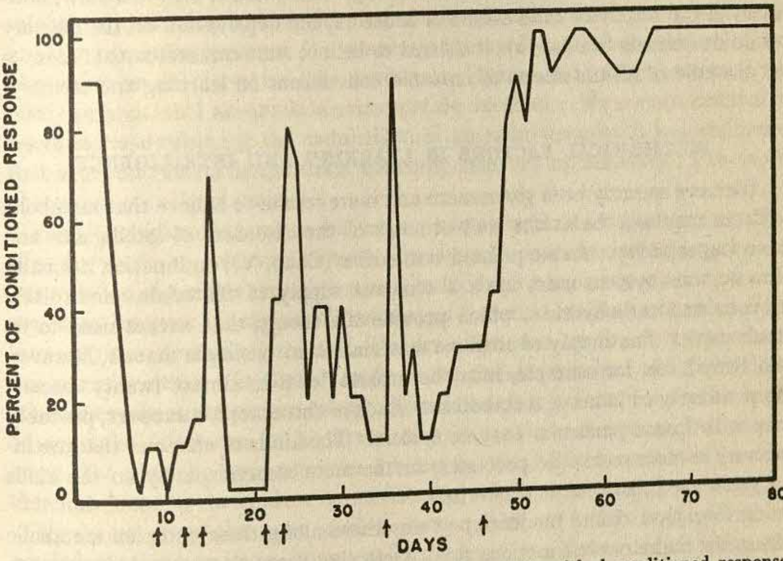

Fig. 166. Temporary and permanent restoration of an extinguished conditioned response produced by injecting 10 units of insulin per kilogram at the times indicated by the arrows. (*After E. Gellhorn and H. Minatoya. The effect of insulin hypoglycemia on conditioned reflexes, p.* 165. *J. Neurophysiol.*, 1943, 6, 161–172. *By permission of the publishers.*)

Physiological Basis of Effects of Convulsions. We know very little of why insulin shock or electroshock and metrazol convulsions impair learning and memory. Some time ago the psychoanalysists thought the fear of the shocks and of possible death was the important factor. This is hardly applicable in animal studies, however, for no impairment of learning or retention came from severe electric shocks to the legs of an animal (Duncan). Neither is there any good evidence that any of these shock treatments produce direct damage to the nervous system. No one has ever found any anatomical or histological damage in the brains of animals that could be attributed to experimentally induced convulsions (see Hayes). Gellhorn has a theory that the shock treatments are effective because they stimulate the sympathetic centers of the central nervous system. Another idea is that convulsions and insulin shock cause cerebral anoxia. There is, in fact, good evidence that cerebral anoxia does occur during and right after shock and convulsive therapy (Himwich *et al.*). In view, however, of the relatively mild effects of acute oxygen deprivation on the memory of adult animals (see below), it is hard to believe that cerebral anoxia alone is at the root of all the effects of repeated convulsions on learning and memory.

BIOCHEMICAL FACTORS IN LEARNING AND INTELLIGENCE

We have recently been given more and more reason to believe that metabolic defects may well be at the root of some of the disorders of intelligence and learning capacity. As we pointed out earlier (Chap. V), to function normally the nervous system must have a constant supply of materials, particularly oxygen and carbohydrate, which provide the energy that nerves need to do their work. The supply of all these materials is not a simple matter, however. Carbohydrate, for example, must be broken down in almost twenty discrete steps to be used in nerve metabolism. Each of these steps, moreover, probably depends upon a particular enzyme system. The kinds of enzymes that are involved in such metabolic processes, furthermore, depend partly on the kinds of genes the individual has inherited.

Obviously, a defect or deficiency anywhere along these complex metabolic lines can make nerve functions fail. Defective genes, for example, can mean inactive enzymes. Then too, even when enzymes are normal and adequate, they must have the right coenzymes with which to work, and these often must be gotten in the diet (vitamins) or must be synthesized in the body by complex metabolic processes. Finally, enzyme activity adequate to meet the demands of the nervous system requires the right set of conditions in the internal environment. As you will remember, changes in pH and temperature, inadequate substrate materials, or the presence of inhibitors can make the difference between normal and abnormal metabolism.

With these facts in mind, research workers have been making an effort to find the specific genetic, metabolic, and dietary factors that may lead to disorders of intelligent behavior. As usual, it is very difficult to find ways of getting at the problem in man, and to do studies of feeble-mindedness. Many have turned, therefore, to experimental attempts to improve or impair the learning capacity of animals by interfering with their normal metabolic processes. Even here, however, they have met their problems, for the nervous system is very well protected, and it is hard to make artificial changes that will affect it.

Feeble-mindedness. Despite the difficulties, however, we can put our finger on several metabolic disorders that are important in human mental deficiency. The outstanding example is the case of *phenylpyruvic oligophrenia,* a rare type of disease which accounts for only about 0.1 per cent of the population of feeble-minded (Haldane). As we pointed out earlier, this disease is marked by the excretion of phenylpyruvic acid in the urine. Normal people can convert phenylalanine, an essential amino acid, into phenylpyruvic acid and then oxidize the phenylpyruvic acid to carbon dioxide and water. In this type of feeble-mindedness, however, the metabolic process is apparently blocked after phenylalanine is converted to phenylpyruvic acid, and large amounts of phenylpyruvic acid accumulate and must be excreted. We do not know the enzymes responsible for the metabolism of phenylpyruvic acid, but we know that a genetic defect keeps them somehow from acting normally in cases of phenylpyruvic oligophrenia.

Familial studies of a large number of cases leave no doubt that phenylpyruvic oligophrenia is an inherited disease (Jervis). It depends, in fact, upon the transmission of a single recessive gene. Individuals possessing one normal and one defective gene are apparently normal, although it has been suggested that they are prone to senile dementia. The dramatic cases are those which possess two recessive genes. In these cases both the metabolic failure and the feeble-mindedness show themselves clearly. We do not know directly how this kind of metabolic defect can impair functioning of the nervous system, but we do know that phenylpyruvic acid can inhibit the synthesis of acetylcholine and therefore probably can reduce nerve function to a very low level.

We do not have the same kind of story yet about other kinds of feeble-mindedness. We do know, however, that many types of mental deficiency are inherited. It may be that future research will work out the mechanisms of inheritance in these cases and be able to point out specific metabolic defects underlying mental deficiency. There are, on the other hand, many types of feeble-mindedness that are caused either by brain injury at birth or by something going wrong with the metabolic machinery early in development. *Cretinism* is an outstanding example of early metabolic failure and can be traced to the thyroid gland not functioning enough during development. The thyroid hormone can do wonders for such cases if given early enough. Another type of mental deficiency that may be the fault of metabolic failure is *mongolian idiocy.* We know hardly anything about the causes of this disease except that it happens more often in children born when their mothers are relatively old. It is interesting, however, that cretins and mongolian idiots, as well as phenylpyruvic oligophrenics, have defective cerebral metabolism. Careful studies of the respiration of brain tissue of these defectives show that their brains are incapable of using normal amounts of oxygen and carbohydrate (Himwich *et al.*).

Effects of Anoxia. Partly because some individuals do not seem able to use normal amounts of oxygen and partly because we know how important oxygen is in nerve function, many investigators (see Shock) have become interested lately in the effects of oxygen deprivation on learning and intelligence. In man, they find that reducing oxygen intake only mildly has hardly any noticeable effect, but severe oxygen deprivation markedly impairs judgment, perception, psychomotor performance, and intelligence-test scores. Just about the same thing happens when rats are tested in a pattern discrimination problem in a decompression chamber. When the oxygen tension is as low as 7.5 to 9.5 per cent the rats cannot learn the discrimination in 10 days of training, but when the oxygen supply is returned to normal they improve steadily with practice (Shock and Scow).

Repeated Exposures. When animals repeatedly suffer oxygen lack and then are put back in a normal atmosphere, their ability to learn mazes depends on how much total anoxia they experienced. Windle and his collaborators have exposed guinea pigs to simulated altitudes of 23,000 and 30,000 ft., 6 hr. at a time, for accumulated periods of from 100 to 400 hr. With exposure to simulated altitudes of 23,000 ft., animals remembered a maze habit about as well as normal animals, although those that were exposed for the longer periods tended to do slightly more poorly than the normal ones (Sola *et al.*). Exposures to simulated altitudes of 30,000 ft. for 100 hr. did not impair retention of a maze habit, but much longer exposures greatly impaired performance.

Anoxia at Birth. Asphyxiation at birth seems to have about the same sort of effect on human behavior. Schreiber made a study of about 250 mentally deficient children. About 70 per cent of them had suffered severe anoxia at birth, whereas the incidence of such asphyxia is only about 5 per cent in a normal population. Inferior neural development could, of course, be a cause as well as an effect of asphyxia at birth, and to check on that possibility Windle and Becker turned to effects of experimentally induced asphyxia at birth on the later learning of guinea pigs. Animals asphyxiated at birth were inferior in learning capacity when tested from 2 to 8 weeks after birth. They were able to run the maze as fast as their litter-mate controls, but they consistently made more errors.

Neural Damage. One interesting point that comes out of all these studies is that, in general, where there is impairment of intelligent behavior as a result of severe anoxia, there is usually some direct damage to the nervous system. There are a few exceptions to this generalization, but not enough to demonstrate that anoxia can impair learning without causing brain damage. For example, exposure to the simulated altitudes of 23,000 ft., which had no effect on learning, had no measurable effect on brain tissue. On the other hand, both neonatal asphyxia and long exposure to simulated altitudes of 30,000 ft. produced widespread damage to brain cells and often led to signs of neurological defect other than the impairment of learning (Windle and Jensen). Many of the animals subjected to severe anoxia and many of the mental defectives in Schreiber's study above suffered from paralysis, hyperirritability, fits, and impaired sensory capacity. The guinea pigs used in the maze studies, on the other hand, recovered from observable neurological symptoms or else never developed them. It is very likely, however, that some of the impairment of performance reported in these studies is not just something wrong with memory but also with sensory and motor capacities.

Endocrine Factors. As we have already mentioned, both thyroid deficiency and an excess of insulin do a great deal of harm to learning and intelligence. Most experimental attempts, however, to improve or impair learning and intelligence by hormone injection or endocrine extirpation have failed. Neither partial adrenalectomy nor the injection of adrenalin, for example, have any appreciable effect on the learning ability of adult rats. Similarly, no observable changes in maze-learning ability follow castration or hypophysectomy in adult animals. Most experimental attempts, finally, to alter learning ability by thyroidectomy or administration of thyroid hormone have failed to produce any positive results.

There are a few noteworthy exceptions to these statements. For one thing, partially removing the thyroid of rats *at birth* impairs learning, as we might expect from what we know about cretinism (Scow). More interesting, perhaps, is the fact that adult animals given a thyroid depressant, allyl thiourea, are much poorer maze learners than control animals. On the surface, this finding appears to be in conflict with the reports that thyroidectomy does not affect the learning ability of adult animals. It probably is true, however, that chemical depression of thyroid function causes a more complete state of thyroid deficiency than surgical extirpation of the gland.

Positive results have also been reported following the administration of moderate doses of adrenal cortical hormones to rats (Riess). In this study, the animals that got injections of cortical steroids learned a maze with fewer errors than the control animals. There was no significant difference in the time scores, however. The investigator who did this experiment suggests that adrenal cortical hormones facilitate learning because they promote the metabolism of carbohydrate, upon which nerve function so crucially depends.

The Effect of Drugs. There are a good many studies of the effect of various drugs upon the intelligence and learning ability of animals and man (see Shock). In general, although drugs like benzedrine and caffeine may speed up performance for a time, they do not produce any marked effects on intelligence-test scores or learning. Similarly, depressants like phenobarbital and alcohol in moderate doses may impair performance temporarily, but they do not have any particular effects on intelligent behavior.

NUTRITIONAL FACTORS

As you might expect, a lot of effort has been given to the problem of nutrition in learning and intelligence. One of the earliest studies was of the effects of a severe regime of food deprivation of rats for as long as 100 days after weaning (Anderson and Smith). Actually, three groups were used in this experiment. One was a control group. The second was a group of animals kept at almost constant weight by limiting their food intake. The third was a group stunted by feeding it a diet in which the only protein source was gliadin. No significant differences in maze-learning ability were found between these groups when the animals were tested either right after the period of stunting or after a long period of refeeding. The same negative results came out of a similar study in which rats were kept almost at birth weight until they were thirty days old (Biel). Apparently, then, severe food deprivation, even to the point of stunting growth, has no effect on either the rat's learning ability or its capacity to perform in the maze situation.

Proteins. Taking the lead from these older experiments, Riess and Block tried to see what depriving animals of particular foodstuffs does to their maze learning. They allowed rats all the food they would eat but restricted them to very small amounts of certain amino acids. One group of thirty-day-old rats was deprived almost completely of the essential amino acid, lysine. A second group of the same age was similarly deprived of cystine, which is not an essential amino acid but which can serve to "spare" some of the ones that are essential. When these rats were tested for maze learning after thirty days of such deprivation, both the deficient groups were inferior to their litter-mate controls. The deficient animals did not differ significantly from the controls in separate tests of activity and motivation, however, so we know that the deficiency was one of learning ability, not one of sensory or motor performance.

Along similar lines is an experiment by Zimmerman and Ross. They fed rats extra rations of proline or glutamic acid and then tested them in maze learning. They found that such rats did better than normal animals. Rats fed glycine, another amino acid, however, were as poor as, or worse than, the control animals. Other investigators, however, have failed in several different experiments to duplicate the findings with glutamic acid. In fact, in one study Stellar and McElroy carried out as closely as possible every detail of Zimmerman and Ross's experiment with glutamic acid. Their rats were fed the same diet, run on the same maze, and subjected to the same experimental program. The only exception was that they used a different strain of animals. As it turned out, they were unable to discover any beneficial effect of feeding the animals an excess of glutamic acid.

The only way to account for this disagreement at the present time is to assume that Zimmerman and Ross's animals were defective animals and required excessive amounts of glutamic acid for normal functioning. Supporting this possibility is the fact that their control animals made far poorer scores in maze learning than other untreated animals studied in the same maze situation.

In fact, their improved animals did not perform much better than the controls in Stellar and McElroy's experiment. The way to follow up on the possibility, of course, would be to get animals from the strain of Zimmerman and Ross for further study. Unfortunately, however, they seem to have become extinct.

That is not the end of the use of glutamic acid in the study of intelligent behavior. Zimmerman and his coworkers have extended their work to studies of human feeble-minded patients. They report that feeding large amounts of glutamic acid to feeble-minded children improves their performance on intelligence tests. Unfortunately, however, the gains in intelligence quotient (IQ) that they report are small, and they have no adequate control group to show that similar gains would not occur without specific glutamic acid therapy. In the experimental group they found an increase of about 7 points in the Stanford-Binet IQ over a 6-month period of treatment. The control group, showing no gain, was a heterogeneous group of feeble-minded children whose initial and final IQ's were compared over a period ranging from 6 months to 8 years. Obviously, differences in practice effects and nonmedicinal treatment of the patients in the interval between tests might well account for the differences they report.

B Vitamins. Perhaps the clearest cases of diet affecting intelligence come from the study of the B-complex vitamins. In a series of experiments by Poe and others, animals deprived of B-complex vitamins in their first weeks of life later showed marked decrement of learning ability. The investigators depleted young rats of B vitamins during the second week of nursing by feeding their mothers a vitamin-B-deficient diet. After weaning at the fourth week, the offspring were maintained on the same deficient diet until they were 6 weeks old. The young were then allowed to have a complete diet for 1 week, after which they were tested in a water maze. The control group, made up of litter mates, nursed with foster mothers who always had a complete diet, and the young themselves were never deprived of any vitamins later in life. In both the original maze test and a test of relearning over a month later, the experimental animals made more errors and had higher time scores than the controls. The results were the same when, finally, the animals were tested in a new maze 1 week after the relearning series.

Thiamin Deficiency in Infancy. Of all the B vitamins, thiamin was the one most responsible for the effects in this study. We know that because a new group of animals deprived only of vitamin B_1 (thiamin) performed almost as poorly as the group deprived of the total B complex. A third group of animals deprived of vitamin B_2 was poorer than its litter-mate control group, but it could do much better than either the thiamin-deficient or the B-complex-deficient animals. It is reasonable, moreover, that thiamin should be important in learning ability, for as we already know it is a coenzyme in the metabolism of pyruvic acid. Apparently the deficient animals were unable to metabolize enough carbohydrate to maintain the normal functioning of the nervous system.

These experiments have been confirmed and extended by O'Neill. He reared rats on a thiamin-deficient diet just as Poe and his group did. In his study, however, he had several groups of animals that were allowed graded amounts of thiamin. One group had between 2 and 3 micrograms of thiamin daily, a second group received 4 to 6 micrograms, a third received between 10 and 15 micrograms (normal requirements), and a fourth group was allowed from 100 to 200 micrograms of thiamin daily. The ability of the deficient animals to learn a water maze was not so good as that of the controls receiving the normal daily requirement of thiamin. The group that was given the excessive amounts of thiamin, on the other hand, was superior to the control animals. Apparently, then, amounts of thiamin in excess of what is required for normal growth can improve the functioning of the nervous system of young animals.

Thiamin Deficiency after Infancy. We have been talking all along about thiamin in the diet of young animals. Indeed, thiamin is not very important in the learning ability of older animals that have had a normal diet during nursing. In a study that paralleled O'Neill's in almost every detail, Lush studied rats started on the experimental diets on their twenty-second day of life. Neither thiamin deficiency nor adding thiamin made any difference in the maze-learning ability of any of her groups of animals. We have another report along the same lines, that allowing forty-day-old rats an extra 100 micrograms of thiamin daily for a 4-week period has no effect on their maze-learning ability (Marx).

Similar studies have been attempted with human beings, but only one, so far, claims that adding thiamin helps learning and intelligence (Harrell). In this study, children from an orphanage were divided into two matched groups. One was fed 2 mg. of thiamin daily while the other received a daily placebo. After 1 year of experimental treatment, the two groups were compared on a series of tests. It is true that the thiamin-fed group made greater gains on most of the tests used, but in most cases these gains were not statistically significant. The group that was fed thiamin, furthermore, was almost invariably the poorer of the two groups in the original matching. Since the children were all below average intelligence and the tests used were not highly reliable, one can consider the greater gains of the thiamin group as statistical artifacts rather than real differences.

Supporting this contention are some other results of experiments in man. In one study, supplementing a group of underfed children with liberal amounts of B-complex vitamins had no beneficial effects on their intelligence-test performance (Balken and Maurer). Similarly, in a study of identical twins, it turned out that supplementing one member of each pair with thiamin did not alter their Binet scores (Bernhardt *et al.*). Finally, depriving young men of thiamin had no appreciable effect on their rate of learning, although their performance on speed tests was somewhat impaired (Guetzkow and Brozek).

PERSONALITY DISORDERS

The last, and in many ways the most difficult, of the kinds of disorder with which we shall deal are those of personality. That factors in the environment and in the life history of an individual have a lot to do with many disorders of personality is not to be denied. We have, on the other hand, good reason to believe that physiological factors, and particularly metabolic defects, often play a major role in causing personality disorders. Without, therefore, intending to belittle the social and environmental causes of such disorders, let us take up what we know about their physiological backgrounds.

The Difficulties. We need to make some excuses for what we do and do not know. One of the chief difficulties is that animals do not have personalities—at least, not any that compare with those of people. We do not have to get down to fine points to see that the complex social patterns, thoughts, judgments, and perceptions that make up personality are not plentiful in animals. Therefore we cannot get to work on personality disorders by turning to animals, as in other problems that we have faced. We are stuck with man, the clinical data we get concerning him, and the very limited experiments that are sometimes possible with him. With these handicaps it is going to be a long uphill effort before we have a really satisfying understanding of the physiological basis of personality.

GENETIC FACTORS

Many times in the past people have suggested that the major disorders of personality tend to run in families. This idea has turned up quite often in the study of schizophrenic and manic-depressive psychoses. As you might expect, it is hard to do good genetic studies with characters as complex as psychoses. Even more perplexing, however, is the problem of how to separate the effects of environment from those of the genetic background when the family provides a major part of both of them. Genetic studies of manic-depressive psychosis have been beset by these difficulties. What evidence we have at hand strongly suggests that most of the different types of this psychosis are inherited as dominants (see Penrose). Both environmental factors and other genetic factors undoubtedly influence the development of the disorder.

Schizophrenia in Families. There is little else to say about manic-depressive psychosis, but fortunately we know much more about schizophrenia. Kallmann, more than any other investigator, is responsible for this. He has studied over 1,000 schizophrenics and 9,000 of their relatives. In summarizing his own work, as well as that of others, he leaves no doubt that schizophrenia occurs more often in the blood relatives of schizophrenics than in the general population (see Fig. 167). For example, although schizophrenia occurs in only 0.85 per cent of the population, we find a rate of about 4 per cent in the distant relatives of schizophrenics and one of 10 to 12 per cent among the parents and siblings of schizophrenics. As you might expect, schizophrenia is even more frequent in families where it is known that two individuals have the disease. When only one parent is schizophrenic, for example, about 16 per cent of the children are afflicted, but when both parents are schizophrenic, about 68 per cent of the children are also schizophrenic.

	Incidence of schizophrenia in general population	Incidence of schizophrenia in consanguineous groups related to:										
		One ordinary index case of schizophrenia							Two ordinary index cases		One twin index case	
		Nephews and nieces	First cousins	Grand-children	Half siblings	Parents	Full siblings	Children	Siblings	Children	Dizygotic co-twins	Monozygotic co-twins
Previous morbidity studies of Kallmann	.85	3.9	—	4.3	7.6	10.3	11.5	16.4	20.5	68.1	12.5	81.7
Range of morbidity rates of other investigators	.3 − 1.5	1.4-3.9	2.6	—	—	7.1-9.3	4.5-11.7	8.3-9.7	20.0	53.0	14.9	68.3

FIG. 167. The incidence of schizophrenia (per cent) in the general population and among the blood relatives of schizophrenics. (*From F. Kallmann. The genetic theory of schizophrenia. An analysis of 691 schizophrenic twin index families, p.* 310. *Amer. J. Psychiat.*, 1946, 103, 309–322. *By permission of the publishers.*)

Schizophrenia in Twins. The roles of genetic and environmental factors are even more clearly separated in the study of twins. When the fraternal twins of schizophrenics are investigated, it turns out that they are no more prone to the disease than the siblings of schizophrenics. Of course, this would be expected if genetic factors were the important ones, since fraternal twins are no more alike in genetic background than siblings. On the other hand, among the identical twins of schizophrenics, the incidence of schizophrenia is 81.7 per cent. The interesting thing, too, is that schizophrenia occurs in the fraternal and identical twins of schizophrenics almost as often when they are reared apart in dissimilar environments as it does when they grow up in the same household. On the basis of his studies, Kallmann concludes that the predisposition to schizophrenia is inherited and probably depends upon a specific genetic factor which he believes is recessive. As Kallmann points out, establishing a genetic basis for schizophrenia does not answer the question of what causes individuals predisposed to schizophrenia to develop the disease.

METABOLIC FACTORS

Research workers have been giving a lot of attention to various metabolic factors that might figure in the major personality disorders. Unfortunately, most of the studies do not turn up any positive relationships, and we could serve no good purpose by going into the details of most of them. We can give some idea of the different kinds of approaches that have been taken in this research, however, and point out some of the more promising leads that have been uncovered.

Vitamins and Drugs. First of all, we can cite some of the outstanding examples of personality disorders that are directly attributable to metabolic disturbances. We know, for example, that severe deficiency of the vitamin, nicotinic acid, causes pellagra and that one of the outstanding symptoms of this disease is a rather widespread disorder of personality. Individuals with pellagra are nervous and irritable, suffer from loss of recent memory, and may develop full-blown psychoses with delusions and hallucinations. Nicotinic acid, as you know, figures in the formation of coenzymes that enter into biological oxidations, but beyond that we do not know in particular what it does in the nervous system. We do know, however, that when nicotinic acid is supplied early enough in pellagra it can reverse the symptoms of the psychosis. Feeding this vitamin does no good for people with other types of personality disorder.

Deficiency of thiamin, like that of nicotinic acid, brings changes in the personality. These are mild symptoms of depression, apprehension, or irritability. Neither the absence of thiamin in the diet nor deficiency in any of the other vitamins, however, normally produces severe disturbances in behavior. Feeding large quantities of vitamins to psychotics, furthermore, does no particular good.

It is known, on the other hand, that acute anoxia produces many of the symptoms commonly associated with psychosis. Of course, these symptoms are reversible and quickly pass off when oxygen is restored. Similar temporary effects may be obtained with drugs like mescaline, marihuana, and alcohol. These facts suggest the idea that some disturbance of normal metabolic processes may be one of the important factors in long-standing psychoses.

Metabolic Signs of Psychosis. Further support for this notion comes from the extensive work of Hoskins and his collaborators. In twenty years of research on the biological basis of schizophrenia they have still not solved the problem. They can, however, show a number of ways in which schizophrenics differ metabolically from normal individuals. The most important ones are these. (1) Schizophrenics have significantly lower basal metabolic rates of oxygen consumption. (2) They fail to dispose of lactic acid very promptly after exercise, and they therefore accumulate fairly large amounts of it in the blood. (3) They have a tremendously high tolerance for large doses of thyroxine and insulin. (4) They show much more variability than normal persons in keeping their internal environment constant. The picture is one of failure to adapt as promptly and efficiently as normal individuals do in the face of metabolic stress. It suggests a fundamental derangement of intermediate metabolism.

Physiological Reactions to Stress. More recent work along the same lines bears out this point. Hoagland and his coworkers have found that the metabolic machinery of schizophrenics fails to react to stress with anything like the speed or degree of normal individuals. They have focused attention on the adrenal cortex and have used the excretion of 17-ketosteroids and lymphocyte count as an index of its activity (Pincus *et al.*). Unlike normal persons, the patients do not show a rise in steroid output upon rising in the morning. Neither do they respond with increased output as normal persons do to experimental stress imposed by trying pursuitmeter tasks, exposure to extreme conditions of temperature, or injection of adrenocorticotropic hormones. Of course, in these studies and in Hoskins's work, it can be expected that situations that are stressful for normal persons are not stressful for schizophrenics. An apathetic attitude or withdrawal from reality, however, does not easily explain why schizophrenics fail to react normally to such physiological stimuli as extremes of temperature, thyroid, insulin, and pituitary hormones. Furthermore, in the case of depressives at least, electroshock therapy makes them again respond normally to stress with increased output of 17-ketosteroids when it alleviates their psychiatric symptoms (Hoagland *et al.*).

Psychosis as a Metabolic Disorder. With such data as these in mind, Hoagland comes out with the hypothesis that a disturbance of intermediary metabolism is at the root of psychosis. More particularly, he suggests that the trouble lies in certain enzyme systems which are essential to normal brain metabolism. Since any one enzyme in a complex series of metabolic steps can act as the pacemaker, this notion is not difficult to formulate and test. If the disorder is in a reaction catalyzed by an enzyme in the metabolic systems supporting nerve function, the reaction should become the slowest one of the series, therefore the pacemaker of the over-all rate of metabolism. The only problem, then, is to see whether such a step in metabolism is blocked in psychotic patients, and if so, to identify the enzyme system involved.

Hoagland has, in fact, made this kind of analysis in one type of psychosis and has come out with some very promising results. For his subjects he used several highly psychotic paretics, some partially cured paretics, and several normal persons. His index of underlying enzyme activity in each of these cases was based upon the change in the rate of the alpha rhythms of the brain (see page 545) as a function of change of body temperature during fever therapy. By applying the appropriate chemical equation (the Arrhenius equation) he was able to show two points: (1) a single enzyme pacemaker was in control of the alpha rhythms in all his subjects, and (2) the normal, partially cured, and highly psychotic groups had different enzyme systems as their pacemakers. He was able, furthermore, to identify the pacemaker operating in the case of the advanced paretics with reasonable certainty as the cytochrome-cytochrome oxidase enzyme system. In support of this view is the fact that the cytochromes require iron atoms in their coenzymes and iron is not available in normal amounts in the brains of paretics. Furthermore, because the cytochrome-cytochrome oxidase system is important in the rate of cortical respiration, we can expect blocking of the system to impair cortical functions.

Of course, many more studies like Hoagland's will have to be done before we can point to failure of enzyme systems as really basic in psychosis. The importance of this approach, nevertheless, cannot be emphasized strongly enough. With future research we may be able to understand the hereditary predisposition to psychosis in terms of the failure of certain defective genes to provide the organism with sufficiently active enzyme systems to permit normal brain function. An individual so predisposed could be entirely normal until faced with sufficient environmental stress to tax his inferior metabolic system. Others metabolically capable of resisting stress presumably would never break down under the same kind of environmental circumstance.

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CHAPTER XXVI

ELECTRICAL ACTIVITY AND BEHAVIOR

This chapter will not hang together quite so well as some of the others. True to its title, it will deal with the relations between behavior and various electrical phenomena of the body. The phenomena, however, are somewhat unrelated and are not too well understood. They are electrical waves of the brain, electrical changes in skin resistance, and electrical signs of muscular activity. There will be a section on each of these types of electrical activity. At the end there will be a section describing some of the notions mathematicians and engineers have been putting forth lately to explain behavior in terms of electrical activity.

THE ELECTROENCEPHALOGRAM

This fifty-cent word is too long for most people to use, and it is commonly abbreviated EEG. Some prefer the term "brain waves." Each of these terms refers to the electrical beat, rhythms, or waves that can be recorded when electrodes are placed on the cortex or on the skull and wires are led from them through amplifiers to recording devices. Although investigators had reported electrical changes in the brain for many years, it was not until 1929 that Hans Berger came forth with the first thorough account of these brain rhythms. Since then hundreds of papers have been published on the subject. Today we can only bring out the high lights of the work, making the conclusions that seem most important and most securely founded.

THE NATURE OF BRAIN WAVES

Brain waves are usually recorded on paper by an ink-writing or hot-point pen. The paper moves along at good speed so that one can see waves that occur as rapidly as fifty times a second. For many years it was the custom to look at records of brain waves and describe them much as we might describe different people. One record might be "spindles," another "saw-tooth," and so on. These types are still convenient to use, and we shall come to them in a minute. More recently, however, it has been possible to describe brain waves in terms of the spectrum of frequencies they contain, and it is better to take up this matter before talking about types of records.

Frequency Spectra. Waves of any kind can be analyzed into a series of sine waves of stated amplitudes. This is Fourier's theorem, which we took up when we dealt with acoustics. It matters little whether the waves are sound waves, light waves, or electrical waves, the principle is the same. In Fig. 168 you can see such an analysis for the waves of the brain (Gibbs). It extends from very slow waves of less than 1 cycle each second to rather fast waves of 50 or 60 cycles per second. There are some peaks at 1 to 2 cycles, 10 to 12 cycles, 20 to 25 cycles and 45 to 50 cycles per second. The spectrum of brain waves is not always the same—it may vary considerably from time to time and from one individual to another—but the picture in Fig. 168 gives a general idea of what it is like.

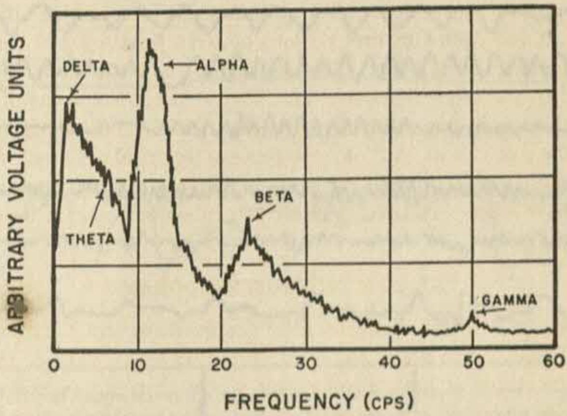

FIG. 168. The frequency spectrum of brain waves. There are four peaks, which have been given Greek names: *alpha waves*, 10 cycles per second; *beta waves*, 20 to 25 cycles; *gamma waves*, 40 to 60 cycles; and *delta waves*, 1 to 2 cycles. Waves of 4 to 7 cycles per second, between the delta and alpha waves, are sometimes called *theta waves.*

Having taken up the spectrum of brain waves, we can now talk more easily about types of records. In Fig. 169 you see examples of six types of records often encountered—which is not all of them by any means. Each of these records brings out some special part of the spectrum displayed in Fig. 168. Each type of record and each part of the spectrum received a name—sometimes several names—and we can now run down through the different parts of the spectrum indicating their significance.

Alpha Waves. The biggest peak in Fig. 168 is at 10 to 12 cycles per second. A record of waves consisting mostly of these frequencies is the one on line II of Fig. 169. These waves are called *alpha waves.* They have always been thought of as the 'normal' waves of the human adult, for they are typical of normal people when they are awake and relaxed. When these alpha waves are missing in a record or are greatly decreased in number it is usually a sign of something—which we shall talk about a little later. It is hard to draw any sharp line for these alpha waves, and people have not agreed on where to draw it, but waves as low as 8 and as high as 13 are about the boundaries of alpha rhythms.

Beta Waves. Berger, the great leader in brain-wave research, called all the waves from about 15 cycles per second upward "beta waves." Not too many people have followed this precedent. In fact, most investigators think of beta waves as those at the peak around 20 to 25 cycles in Fig. 168 (see also line IV in Fig. 169). Frequencies somewhat below that are often called "slow beta waves" and those above it "fast beta waves." In between the beta and the alpha waves are some frequencies between 12 and 15 cycles per second that we frequently see in people during sleep. These appear in trains, as you see them in line III of Fig. 169, and are called "spindle waves." In the spectrum of Fig. 168, on the right, is a small peak between 40 and 50 cycles. For the sake of a name these sometimes have been called "gamma waves," but they lie within the broad band of beta waves and we know very little about them.

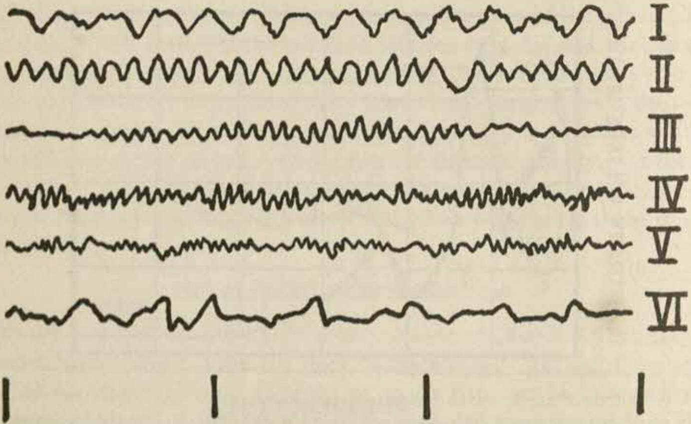

FIG. 169. Six types of cerebral action potentials ("brain waves") recorded from the human skull. I, saw-tooth waves, seen commonly in young children and consisting of 4 to 7 cycles per second; II, Berger's alpha waves, usually between 9 and 11 cycles per second and seen in normal adults at rest (but not asleep); III, spindle waves, between 12 and 15 cycles per second and appearing in trains during sleep; IV, rapid rhythms of 20 to 24 cycles per second, only rarely observed; V, Berger's beta waves, 25 to 35 cycles per second, seen in normal waking adults; VI, large random waves of no particular frequency, characteristic of sound sleep. (*From L. W. Crafts, T. C. Schneirla, E. E. Robinson, and R. W. Gilbert. Recent experiments in psychology. New York: McGraw-Hill,* 1938. *P.* 195. *By permission of the publishers.*)

Delta Waves. As you can see in the frequency spectrum, a large part of the energy of the spectrum is at the low end below 8 cycles per second. The peak of these slow waves is at 1 to 2 cycles per second. Such slow waves are known as delta waves. We see them appearing irregularly in sleep as in the case of line

VI of Fig. 169. Custom varies on the naming of the frequencies in between, *i.e.*, those between 3 and 8 cycles per second (see Lindsley). Some call all waves below 8 cycles "delta waves." Others have made up the name *theta waves* for bands of 4 to 7 cycles per second (see Walter and Walter). Such waves appear under several different circumstances, but are rather common in young children. You see a sample record from a child in line I of Fig. 169. Such a record is sometimes called *saw-tooth* waves.

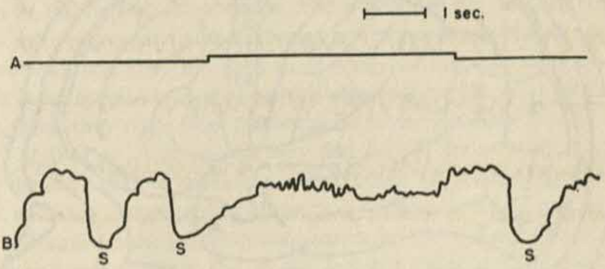

FIG. 170. Bursts of kappa waves during reading. The large waves, *S*, are muscle potentials that come from the eye when it sweeps back from the end of one line to the beginning of the next. The fast small waves superimposed on top of the large slow ones are the kappa waves. (*From J. L. Kennedy, R. M. Gottsdanker, J. C. Armington, and F. E. Gray. A new electroencephalogram associated with thinking, p.* 527. *Science*, 1948, **108**, 527–529. *By permission of the publishers.*)

Kappa Waves. The alpha, beta, and delta waves have been known from the beginnings of electroencephalography, and research has served only to show us when and where they are to be found. Quite recently, however, a new wave has burst upon our horizon—the "kappa wave" (Kennedy *et al.*). It is rather different and perhaps more significant than the other waves. It has about the same frequency as the alpha wave, *viz.*, 10 per second. Its voltages, however, are much smaller than those for alpha, and it appears under conditions quite different from those for alpha. In Fig. 170 is a record of kappa waves appearing in the electrical record of eye movements. The very small waves riding on top of the big ones are the kappa waves.

THE ORIGIN OF BRAIN WAVES

It may seem that there are a few too many names of brain waves—and there are. We must, however, put up with usage as we find it. The names, moreover, make it a little easier to talk about other questions and facts about brain waves. The first of these is, Where in the brain do brain waves come from? Certainly if we knew that, we might be able to see better what they mean and to what use they might be put.

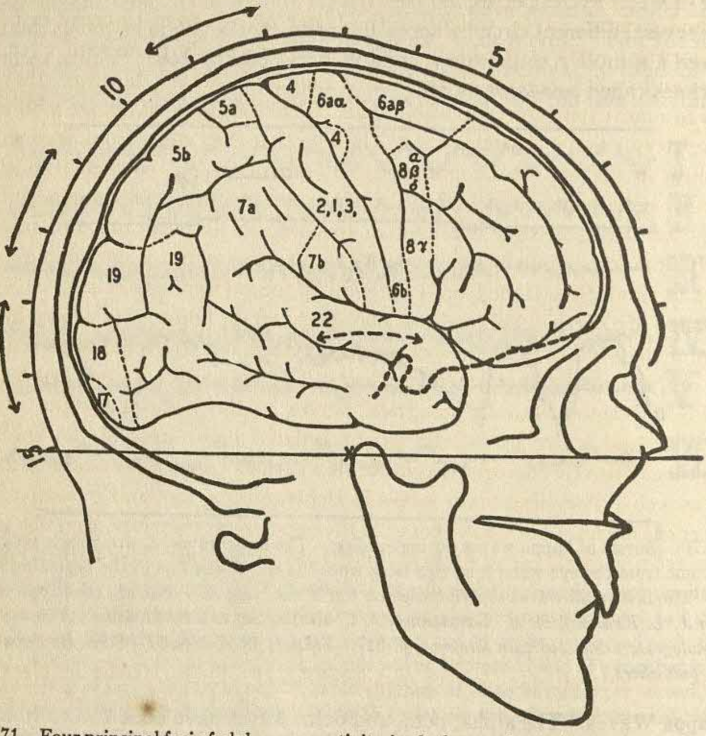

FIG. 171. Four principal foci of alpha wave activity in the human brain (indicated by arrows): the occipital area at the extreme back of the brain, the related area just dorsal to the occipital area, the primary sensory and motor areas, and the temporal area. (*From D. B. Lindsley. Foci of activity of the alpha rhythm in the human electro-encephalogram, p.* 167. *J. exp. Psychol.*, 1938, **23**, 159–171. *By permission of the American Psychological Association.*)

Cortical Areas. By placing electrodes in many different positions on the human skull, investigators have learned that different waves are stronger in different places. In general, there are four foci for the *alpha waves*, and these are marked with arrows in Fig. 171 (Lindsley). One is in the lower occipital region around the striate area, another is in a higher occipital region around area 19 (the parastriate area), a third is in the parietal central region of the postcentral and precentral cortices, and a fourth is in the temporal region. The strongest source of alpha is usually the occipital region, and particularly the upper part of it. For that reason some have thought that alpha is generated in the occipital cortex and carried to the other regions (Adrian and

Yamiguva). On the other hand, these four foci of activity are not clear-cut in every individual. In some another focus may be the stronger, and in some alpha seems to come rather evenly from all parts of the cortex (Lindsley).

There is a different primary locus for each of the other brain waves. The beta and gamma waves, which are the faster waves, seem to come from the more forward parts of the brain. They are particularly prominent over precentral and frontal regions of the brain. Like alpha waves, however, they are found to some extent over the whole skull. The slow delta waves are a bit more of a mystery. Some (Hoagland *et al.*) believe that they come from deep within the brain in the hypothalamic region, but others are not so sure (Lindsley). Certainly delta waves are found in the cortex around areas of lesion and tumor, and as we shall see, they are used in this way to find the place of tumors. Finally, it is too soon to be sure about the kappa waves, but what we know now makes us think they come from the temporal lobes (Kennedy *et al.*).

Tissues of Origin. Although we may find certain brain waves more in one region of the skull than in another, such waves are not restricted to the cortex. They are, in fact, a rather general property of nervous tissue. Long ago Adrian and his colleagues recorded electrical waves in the isolated ganglia of the caterpillar and water beetle and in the isolated brain stem of the goldfish. Since then, neurophysiologists have studied various parts of the brain of mammals as well. They find brain waves in these animals, too, and in some of the subcortical nuclei. They have come to the conclusion, therefore, that electrical waves are a rather general property of masses of neurons almost wherever we find them (see Jasper and Kershman).

Synchronized Activity. Another point is now clear, that brain waves are the synchronized, summated effects of changes in the potential of thousands and usually millions of cells (Adrian and Matthews). Each cell has an electrical wave, and the various cells in a group get into step so that their changes wax and wane together—probably by means of synchronizing mechanisms that we described earlier (page 69). We do not know, however, whether the waves are summations of slow or of fast activity; *i.e.*, we do not know whether bursts of spikes from various neurons make up the brain waves or whether slow continuous changes in potential are the cause (Renshaw *et al.*). There will have to be more research on this point before we can come to a conclusion.

Sources in the Brain. Finally we come to the question of what neurons are working together in brain waves. Where in the brain do the brain waves come from? For some time people believed the brain waves to be of cortical origin. Destroying successively three or four layers of the cortex, for example, abolishes the brain waves in the region of injury (Dusser de Barenne *et al.*). We noticed earlier (page 295), moreover, that when suppressor areas of the cortex are brought into play, they suppress the electrical activity of many other areas of the cortex (McCulloch). Such experiments as these might make us think that brain waves come from the cortex.

Other experiments, however, make it seem that the waves in the cortex are conveyed from lower, subcortical centers. It is possible, for example, to abolish the waves in a cortical region simply by destroying the fibers that project to the region (Walter and Dovey). Brain waves comparable to alpha waves, moreover, occur in the thalamus of an animal that is completely decorticate (Morison and Bassett). Some have seemed to locate some waves in the hypothalamus (Murphy and Gellhorn). So brain waves involve not only the cortex but other centers as well.

Some have had the idea, finally, that a reverberatory circuit between the thalamus and cortex is responsible for brain waves (see Lindsley). We know now that such a circuit cannot be the sole cause of brain waves, because they can go on when no such circuit exists, *i.e.*, in the decorticate animal. The circuit, however, may help. It may modify the rhythm and increase its magnitude by recruiting more fibers at both thalamic and cortical levels. So the notion has some merit. We need a lot more research, however, before we finally clear up the exact mechanisms of electrical waves in the brain.

CORRELATES OF BRAIN WAVES

We shall now take up a number of factors that have been correlated with brain waves. Whenever we speak of correlations, of course, we have a problem of cause and effect: Which of two correlated variables causes the other, if one does? In this case it is well to avoid the question, because we do not know whether brain waves can be the cause of changes in behavior, or vice versa. We shall therefore consider briefly the relationship between brain waves and a number of other factors.

Individual Differences. One of the basic questions about any kind of measure is, How reliable is it? Does a person get the same mark when the measure is used over again? How well does the measure distinguish one person from another? We have the same questions about brain waves. The answers have not been put forth in quantitative terms, but they are fairly clear.

Each individual usually gives a record of brain waves that is fairly characteristic of him, and the trained person comparing many records often can match up records belonging to the same person. Rather extensive studies have been done on twins to see whether the constancy of the brain-wave record is a matter of heredity. In this kind of measure, as in many others, twins are much more alike than are siblings or unrelated persons. We therefore can come to the expected conclusion that both heredity and postnatal life have their parts in the typical record of brain waves.

Age. Brain waves are not only typically different for different individuals, they are not the same for children as they are for adults. You can see that in Fig. 172. At birth there are regular brain waves at about 7 per second in the central regions of the skull. In the occipital region, however, which later is the main source of alpha, there is hardly any rhythm at birth. The waves that appear are rather irregular. After 3 months, however, some regular waves show up in the records. The waves are very slow, *i.e.*, 3 or 4 cycles per second, but they gradually get faster as the child grows older. By 2 years of age, both the occipital and parietal "alpha" waves are about 7 cycles per second, but the parietal rhythm stays a little faster all through the development of the child.

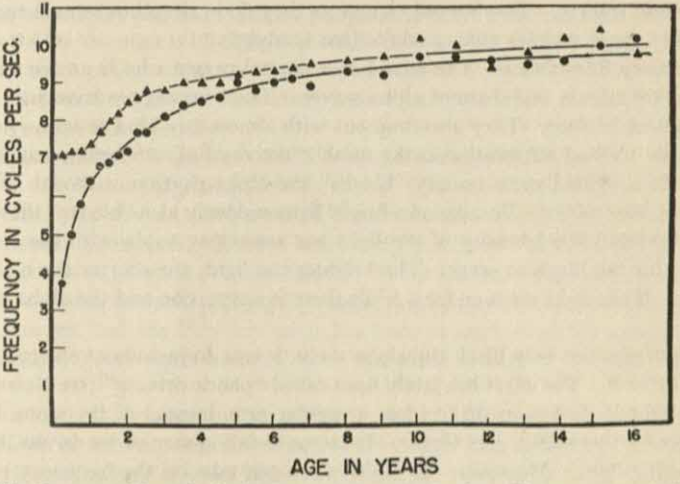

FIG. 172. Increase with age in the frequency of the alpha rhythm. The upper curve indicates the frequency from the central region over areas 1, 2, 3, and 4; the lower curve refers to the occipital alpha rhythm. (*After J. R. Smith. The frequency growth of the human alpha rhythms during normal infancy and childhood, p.* 188. *J. Psychol.*, 1941, 11, 177–198. *By permission of the Journal Press.*)

Finally, at about nine years of age, both rhythms have come to be about 10 cycles per second, which is the typical adult rhythm.

Sleep and Hypnosis. It has long been known that the brain waves change when we go to sleep (see page 359). They change in three stages. The first stage is that of drowsiness or drifting. In this stage people who normally have good alpha waves show somewhat smaller ones; others who tend to have a lot of fast waves when awake show somewhat more alpha. In general, the brain waves get slower in this stage and show more waves of about 4 to 6 cycles per second. A second stage is one of dozing and light sleep. In this stage the record of brain waves shows a lot of "spindle" waves, like those in line III of Fig. 169. These spindles come in bursts, and their frequency is about 14 to 16 per second—sometimes called slow beta waves. The third stage is one of deep sleep. It gives us rather large slow waves of ½ to 3 cycles per second, which come rather randomly. The record looks like line VI of Fig. 169. If a person is disturbed in a sound sleep by a sudden loud sound, there is a reaction in his brain waves called the K complex (Davis *et al.*). This consists of some slow waves with alpha waves (8 to 14) imposed on top of them.

In passing we may touch upon an old question about the relation of sleep and hypnosis. Although they may sometimes look alike, sleep and hypnosis are basically not the same or even very similar. One way of showing that is with brain waves. Brain waves have been recorded in several experiments with hypnotic trances. They do not change as they do in sleep but remain entirely as they are in normal waking adults (see Lindsley).

Sensory Stimulation. The record of a normal person who is awake and relaxed contains a fair share of alpha waves. These waves, we have just seen, disappear in sleep. They also drop out with almost any kind of sensory stimulation. Visual stimulation is the most effective of all. Simply opening the eyes in a lighted room usually "blocks" the alpha rhythm, although after a time it may return. Turning on a bright light suddenly also "blocks" the alpha rhythm, and the intensity of the light has something to do with the time it takes for the block to occur. The brighter the light, the shorter the blocking time. If the light stays on for a while there is adaptation and the alpha comes back.

Light can not only block the alpha wave, it can do just about the opposite, *viz.*, drive it. The effect has lately been called "photic driving" (see Halstead). If a light is flashed or flickered at a regular rate, instead of the alpha being blocked it sometimes gets bigger. It seems to fall in step or be driven by the flickering light. Moreover, the alpha wave can take on the frequency of the flickering light. Thus a normal alpha can drop down to 5 cycles or up to 15 cycles per second when it is driven by flashes of light.

We may hazard a guess as to why the alpha wave is sometimes blocked and sometimes driven. If alpha waves come from many neurons pulsing in step, a sudden stimulus or a steady stimulus can knock them out of step. Impulses coming from the stimulus are scattered in time, rather than in waves, and thus flatten out the record and "block" the alpha wave. A flickering stimulus, on the other hand, sends impulses into the nervous system in waves. If it is natural for the neurons to pulse together anyway, as they do in brain waves, the flickering stimulus just helps them out, thus making them even bigger.

Other stimuli such as sounds, touch, and pain do about the same thing to alpha waves, at least in their respective areas of the cortex, as does light (Lindsley). Coming on suddenly, they all block the alpha rhythm. After they have been on for a while their effect gets less and the alpha wave may return. When auditory stimuli are repeated at a regular rate, they "drive" the alpha rhythm over the auditory region just as flickering lights "drive" the occipital waves. These other stimuli, however, although they have the same general effects as light, are not nearly as effective as light. Perhaps that is because the occipital region, *viz.*, the visual region, is the best source of the alpha waves.

Attention. Many investigators have noticed that brain waves, particularly the alpha waves, seem to be depressed whenever the subject pays attention to anything. It matters little whether he is reading, talking, watching a moving picture, listening to music, or waiting for somebody to flash a light or ring a gong. Any distracting stimulus or any stimulus that gets the attention of the observer blocks the brain waves. There is little doubt about this fact. What it means, however, can be argued. Some think that "attention" is a sort of tensing of muscles and increasing of peripheral stimuli and that such stimulation is the major cause of blocking (Knott, Freeman). Others think that mental activity involves a good part of the brain and thus is likely to get in the way of alpha rhythms because they get along best when the brain is doing little but staying awake (see Lindsley).

Mental Activity. Whatever attention is, it is not very different from mental activity. It is not surprising, therefore, that both mental activity and work block the alpha waves. Give a man a problem in arithmetic to solve and his alpha usually disappears. Or have him sitting quietly and ask him to tell you what is on his mind when you say "Now." When his brain-wave record shows a block in alpha waves, he will usually admit that he has been having thoughts, visual images, and the like—his mind has been at work—but his record will show fairly regular alpha activity when his mind is a relative blank (Travis).

Mental effort, however, not only blanks the alpha waves, it produces two other kinds of waves. One is fast beta waves. Some have reported waves of 40 to 100 per second or even higher when mental work is going on (Berger). There is the possibility that some of these waves are not brain waves at all but rather muscle potentials (see below); but some waves in the beta range, higher than alpha, are no doubt brain waves and appear during mental effort (Travis).

The other wave that comes out in mental effort is the *kappa wave*. This is a relatively recent discovery (Kennedy *et al.*). When a subject is given some problems to solve, the kappa wave appears in the record if the electrodes have been put in the right place on the skull. In fact, kappa waves seem to appear only when a person is thinking or making mental effort. As we said, it is about the same frequency as the alpha rhythm, but there are two ways to distinguish it from alpha. One is that it has much less amplitude than the alpha wave, and the second is that it turns up only when the electrodes are in a region of the skull over the temporal lobe just behind the frontal lobe. We should note, incidentally, that kappa waves can be found in only half the subjects. Why this is true, as well as many other questions about kappa activity, is something for future research to tell us.

Emotional Reactions. Research workers have also been trying to find changes in the brain waves that go along with emotions. There are some changes that we can be sure about and others that are a bit doubtful (see

Lindsley). Certainly emotional reactions, indeed very mild embarrassment or concern, block out the alpha waves. Many investigators have made that clear, and that is what we would expect anyway. Some have found, too, that there are more fast waves (beta) after emotional stimulation than before (Darrow *et al.*). Others find more slow waves, *i.e.*, delta waves, in emotional states.

Although there is some doubt about these delta waves, they are worth more than a passing thought. Hoagland and his colleagues (1938) recorded brain waves from both psychotic and normal people while embarrassing questions were fired at the subjects. The normal people had an increase in delta waves. Schizophrenic patients, however, showed less change than normal people, which is what we might expect. When the questions were repeated, both groups adapted, *i.e.*, their brain waves showed less delta activity.

Unfortunately, however, these results have not been confirmed, and it is possible that the so-called delta waves were not delta waves at all but rather changes in potentials of the skin (Lindsley). We could argue the matter pro and con, but it will not be settled without more research. Like Hoagland, others find some slow waves in people subjected to emotional situations, but they can find them only in the premotor region of the skull (Lindsley and Sassaman). Hoagland got his slow waves best when he recorded from electrodes around the pharynx. He decided, therefore, and with reason, that the slow waves in emotion come from the hypothalamus. Only time will tell.

Personality. A lot of effort has been put to the question of whether brain waves have anything to do with personality. We do not have space here even to mention the names of the various studies, let alone give them any detailed description. In some studies it looks as though there is some connection; in others it does not. In general, those studies that use tests to measure traits of personality have had poor luck with any relationship to brain waves. The studies in which more thorough, but more subjective, means of sorting out traits have been used, such as those used in psychoanalysis, have come up with a positive relationship between brain waves and personality (see Lindsley).

To the extent that there is a tie between personality and brain waves, it is what we might expect from what we have already said. Alpha waves are more in view in the passive, reposed individual and less in evidence in active, fidgety people. This ties in with the ways in which alpha waves are blocked. Sensory stimulation, attention, mental effort—all block alpha activity. People whose minds are working every minute should not, therefore, have much alpha activity. Those who stay relaxed, passive, and dependent, with their minds something of a blank, should have a good deal of alpha activity. So goes both the theory and the facts that are sometimes reported. There probably is such a trend, but it is only a trend and a very small one. A really complete, well-controlled, and trustworthy study on this subject is yet to be made.

BRAIN WAVES AS SIGNS OF DISORDER

This is not the place to go into all the ways in which brain waves can be used in medicine and neurology. Some of them have little to do with physiological psychology. There are, however, three ways in which brain waves have been used as signs of neurological or psychiatric disorder that deserve brief notice.

Brain Lesions. If brain waves never do anything else for us, they have earned the effort that has been put to them by their value in locating lesions of the brain. Small lesions are hard to find either with brain-wave methods or with any other, but large gross lesions of the brain often can be found by putting electrodes at many points on the skull and comparing the records of brain waves obtained at each pair of points. In the region of the lesion, especially around its borders, the brain waves are abnormal, and in any one of a variety of ways. There may be isolated fast "spikes," slowing of the alpha waves, "saw-tooth" wave forms (see line I, Fig. 169), around 4 to 7 cycles, and very slow delta waves. Any abnormal activity is an occasion for a second look at the region from which they come. In general the slow waves, particularly 1 to 3 cycles per second, are the surest signs of damaged tissue.

Epilepsy. Brain waves can also give signs of epileptic disorders (see page 522). Everybody who has recorded brain waves in epileptics agrees to that. Investigators have some trouble, however, in saying just how brain waves can signal such disorder. They vary among themselves in the signs they use. In general, brain waves that are either too fast, too slow, or both are epileptic signs. If the waves are "spike-and-dome," *i.e.*, a series of alternating spikes and slow waves, they are signs of the *petit mal* seizure. This sign usually appears in the frontal and precentral regions when it is present. Brain waves that are very fast and very large, usually coming in bursts, signal *grand mal* attacks—convulsions of the whole body. Another type of epileptic attack, the psychomotor attack, in which a person does things impulsively, go with large slow waves of 3 to 6 cycles per second (Gibbs and Gibbs).

Using brain waves to diagnose epilepsy is a science and an art of its own. Expert eyes can see signs of epilepsy in a record that looks normal to the novice. We cannot follow all the bypaths of the subject here. The important point is that brain waves do help spot epilepsy. They are not infallible, and there are indeed many normal people who have epileptic brain-wave patterns. The telltale waves, however, occur thirty times as often in epileptics as in normal people, and that is extremely helpful.

Psychiatric Disorders. One can always hope, and for a while some did, that psychotics may be recognized by their brain waves. They cannot! After studies too numerous to mention, it turns out that brain waves are not very good signs of mental disorder. In schizophrenia there is no consistent relation. It looks as though schizophrenics have more abnormalities of their brain waves than normal people, but not in any one conspicuous way. Their brain waves seem to be a little faster, more irregular, and somewhat weaker in amplitude. Some have reported that *depressed* manic-depressive patients show rather good normal alpha waves but that *manic* manic-depressive patients have abnormal fast alpha mixed with beta and somewhat irregular waves (P. A. Davis).

So far, brain waves are better signs of behavior disorders in children than they are of any other kind of psychiatric disturbance (see Lindsley). The vast majority of children who are delinquents and behavior problems show something wrong with their brain waves. Most of them have a great deal of slow activity between 3 and 6 per second, and some also show some kind of damage to their cortices. About that there is little question. The question of cause and effect, however, can be argued. Perhaps it is brain lesions that make children problems and also give them abnormal brain waves. Or perhaps the brain waves are linked with personality traits and emotional disorders that cause their social delinquency.

THE PSYCHOGALVANIC REFLEX

From brain waves we can go now to another kind of electrical activity of the body. This is usually called the psychogalvanic reflex or the galvanic skin response. Since these names are long and awkward to use, their abbreviations are handy—PGR or GSR. Whatever the name, the phenomenon has been known since 1879—which is quite a long time. It can be recorded with a simple galvanometer or almost any kind of voltmeter.

Methods of Measurement. There are several things one can record, and it is well to get them straight. If we put some electrodes on a subject—almost anywhere will do, but one in each hand is common—and apply a small voltage, we can measure a resistance across the electrodes. The resistance is apt to be of the order of several thousand ohms. This resistance is called a static resistance or resistance level. It is not the PGR or GSR. If some stimulus comes along, however, say, an unexpected gunshot, the resistance between the electrodes goes down for a time. It is this change in resistance, not the static level of resistance, that is the galvanic skin response. The change is relatively slow, taking a few seconds to build up and to decline. In general, the change of resistance in the GSR is proportional to the static level, but that is not necessarily so (see Landis, Darrow, McCleary).

The Source of the Reflex. It is still not certain just what happens in the GSR. A long argument has raged about it. Some believe the GSR comes from changes in blood vessels in the region of the electrodes, a few have thought the GSR is really a response of muscles under the electrodes, and many think it comes from the activity of the sweat glands. The last of these notions is probably correct. There is not time to say why, but a great deal of evidence points in one way or another to events connected with the sweat glands (McCleary). Sweating itself is not the cause of the response, but some neural or chemical activity in the skin that precedes sweating probably is.

We know something, too, about the central mechanisms of the GSR (see McCleary). It starts in the premotor area (area 6) of the cortex. Electrical stimulation of the premotor cortex brings out the reflex, and conversely, removing the premotor area abolishes the reflex. The premotor area, you will remember, is a headwater of the extrapyramidal system. It is involved in the postural preparation for actions. It is interesting that the GSR goes along with this kind of function. We might add, too, that some place in the hypothalamus, in the region of the tuber cinerium, probably has something to do with the reflex, but we are not sure just what.

The Reflex and Behavior. It is hard to say just what the galvanic skin response does and does not indicate, but it certainly is a very sensitive sign of something going on in the nervous system. The response occurs whenever a person is the least bit emotional, and it will usually show up in a record even when there is no other sign of emotional response. For that reason the galvanic skin response became popular some time ago as the "lie detector." Although it is not perfect, it serves the purpose well and, together with other evidence, can point to the situations that make a person feel "guilty" and embarrassed. So the GSR is a good and sensitive sign of emotional and autonomic response.

The trouble is that it may be too sensitive and that it may signal too many different events. Many years ago some investigators believed the GSR to be a certain sign of emotion (see Landis). They soon learned, however, that the GSR comes out in all sorts of situations, when people are surprised or startled, when they get an idea suddenly, and when they are expecting something to happen. It may occur as a person prepares to make a movement or do something. In fact, a good general statement about it is that it comes out whenever a stimulus or idea sets a person in readiness or expectancy of something happening (see Darrow).

The GSR has been used in many different kinds of research. In some it has been recorded at the same time as brain waves. It has often been used by students of learning as a simple response that can be conditioned easily. More and more in recent years it has come into use in experiments with personality, because it is such a good sign of emotional response. Indeed, some recent research makes it appear that people can be conditioned to give GSR's to emotional stimuli so weak in intensity or so brief in duration that the person cannot tell what the stimulus is. Thus the GSR can serve as a sign of "subception"—a new word that has been coined to mean "unconscious perception" (McCleary and Lazarus).

ACTION POTENTIALS OF MUSCLE

We come now to the third kind of electrical activity that can be picked up in our bodies. This is the action potential of the striped or skeletal muscles. Like brain waves and the galvanic skin response, the action potential of muscle is strong enough and spreads far enough in the tissues so that electrodes put on the skin can detect it. For this reason and because no surgery or unusual experimental conditions are required, the action potential has been a rather popular measure in recent years.

The Nature of Muscle Action Potentials. The brain waves, skin responses, and muscle potentials have different frequencies. The galvanic skin response is very slow, taking seconds to build up and seconds to decay. The brain waves, as we have seen, are somewhat faster, for they run from about ½ to 50 cycles per second. Fastest of all are the muscle potentials. These are much like nerve action potentials and have spike potentials that last only a millisecond or less and come again and again hundreds of times a second. It is the different frequencies of these different potentials, and electrical recording systems designed to match them, that let us keep the different potentials straight.

In the case of the muscle potentials, however, we are not interested in the many spikes that could make up the record. We want some kind of picture of the total activity of a muscle rather than a count of its individual impulses. We can get that picture by using the appropriate apparatus—apparatus that lets all the individual spike potentials add up into a large wave. This wave, which is rather slow, shows how the tension in the muscle builds up, reaches a peak, and then gradually dies down. By putting electrodes around the body over any particular muscle we can record activity in most of the muscles of the body.

Action Potentials and Behavior. There is no exciting story to tell about muscle action potentials. They do just about what we can expect of them. When muscles contract or relax, the fact shows up in the record. The main use of the action potentials is to study patterns of muscle contraction in different kinds of movement. Stetson and his colleagues, for example, have been interested in such movements as throwing balls, swinging batons, steering, and the like. By using action potentials they have gotten some idea of what is going on in each of several muscles involved in these movements. From their analysis they have come to some conclusions about movements, but these conclusions are not a proper subject to talk about here.

Muscle action potentials have some advantages over other ways of recording movements. For one thing, we often do not encumber or impede movement so much by putting some electrodes in the proper places as we would by tying on strings or levers with which to record movement. For another, action potentials are often rather sensitive and even accurate signs of the patterns of behavior. In one recent experiment, for example, in which people turned knobs to keep a marker on a moving target, action potentials measured just about as well the merits and demerits of different conditions as did measures of time taken to get on target or the number of errors made. This experiment is illustrated in Fig. 173 (Jenkins and Connor).

Action Potentials and Thought. The most exciting place in which the action potential has come to the fore is in the question of consciousness. Is it central or peripheral? Do we think with our brains or with our finger tips? Debate raged on this question many years ago, and many different kinds of experiments put it to the test. One was to see whether muscles contracted whenever people had thoughts or indulged in "conscious" processes. Before the method of action potentials came on the scene, very crude mechanical methods of recording muscle movements were tried. Naturally, they did not give very clear answers to the question (Thorson), but the action potentials used in later experiments did.

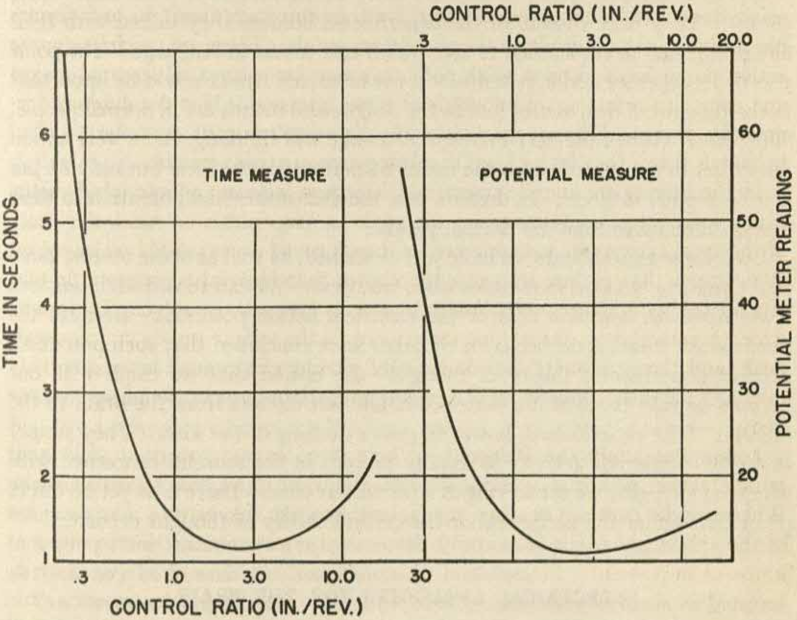

FIG. 173. Action potentials as a measure of behavior. On the left is a graph of the time taken to get a marker on a target by turning a knob. On the right is the action potential in arbitrary units on a meter. Note how nearly alike the two measures are. On the abscissa is the ratio of inches of movement of the marker for each revolution of the knob. (*After Jenkins and Connor. From A. Chapanis et al. Applied experimental psychology. New York: Wiley,* 1949. *P.* 328. *By permission of the publishers.*)

In one series of experiments, subjects carried on mental tasks that the experimenter gave them to do (Jacobson). At the same time their muscle movements were picked up and recorded by way of the action potentials. If subjects were too tense it was hard to see signs of mental effort in the action potentials, but when they were thoroughly relaxed it was a different story. Contractions of their tongues and lips could almost always be detected when they were thinking of talking, doing mental multiplication, imagining the word 'everlasting,' or thinking of the words of a song. The pattern of the potentials for such "unseen" responses was just about the same as when the subject did the tasks "out loud." It also appeared in the same set of muscles—those of the tongue in thinking in terms of words, those of the eye when thinking of visual objects, and those of other parts of the body according to the kind of thought.

We have another study along this line, which was done with deaf-mutes (Max). They were chosen for the experiments because they talked with their hands and had never learned to use mouth and throat in language. The point was to see whether action potentials in the arms and hands would be important in the thought of deaf-mutes just as the tongue and mouth are in normal people. They were. When the deaf-mutes were awake and thinking, there were action potentials in the records from the hands 84 per cent of the time but only 31 per cent in normal subjects. In dreams, too, the deaf-mutes had potentials in their hands much more than did normal people.

Both these experiments we have just described, as well as some others, show that there are tensions in muscles when we think. We can record such tensions if we have the sensitive sign of the electrical action potential. Because the tensions are there, some behavior theorists have concluded that such potentials support a peripheral theory of thought—the notion that we think with our muscles or that thought is a series of in-and-out circuits from the brain to the muscles. The experiments, however, prove nothing of the kind. They simply show that muscular activity is usually present in the muscles concerned with whatever thoughts we are having at a particular time. There is as yet no direct proof that either the peripheral or the central theory of thought is correct.

ELECTRICAL ANALOGIES FOR THE BRAIN

Science has its fads just as people do, for it is people who make science. The fads are in ideas and in lines of research, however, and they seldom are completely wrong. Since the Second World War, a fad has been gaining ground that began well before the war. The idea is to liken the brain to a set of electrical circuits, or more particularly to a computing machine, and then to see how many of the problems of human behavior could be solved and understood if the analogy could hold true.

Background. Attempts along this line began with a group in Chicago who called themselves mathematical biophysicists (Rashevsky). At first they simply tried to devise theories for how the brain worked in behavior by using the sort of mathematical procedures that have long been in use in theoretical physics (Householder and Landahl). At the same time, however, the communications engineers were devising equipments for "packaging" information in highly complex circuits, the mathematicians and electrical engineers were building more and more complex computing machines, and psychologists during the war faced problems of human beings operating such devices as gun directors and servomechanisms. All these various trends in thinking and theorizing came to a head when Wiener dubbed the new field cybernetics and published a book under that title.

It is hard to tell how far the fad will go or even whether it is a fad. At present the field of cybernetics is mainly a set of analogies between electrical devices and the brain. Analogies never prove anything, but they sometimes are very stimulating and lead to something else that can be proved. Some of the ideas of cybernetics are easy and convenient ways to think about physiological functions, even if they are not correct. We believe it is worth while, therefore, to put down a few of the central notions of the field.

The Brain as a Digital Computer. Mathematicians and electrical engineers design computing machines in many ways. One way, the way that is used in some of the vastly complex modern computers, is to use thousands of relays. Each relay can be either open or closed and thus carries along "all-or-none" information. Relays can be arranged in banks so that the action of one relay sets off a second relay and that in turn trips another relay, and so on. Such computing machines, designed with all-or-none relays, are called *digital computers.*

It is easy, of course, to make an immediate analogy with the brain. Each neuron, we know, obeys an all-or-none law. It is either on or off. Thus it is just like a relay in a computer. We have billions of neurons in our brain—more than have been put into any physical computers—and they are arranged in various sorts of banks and circuits so that one neuron going on can set off another neuron, and so on. Having likened the neurons to relays and the brain to a computing machine, we can go on with the analogy and see what kinds of circuits may be in each and how they may function.

The Reverberating Circuit. We have already made a good deal of the closed loop, or reverberating circuit, in the nervous system (page 75). All over the nervous system we run into such circuits, which once started can continue themselves indefinitely until some activity comes along to stop them. The cyberneticists make much of the reverberating circuit. Besides endowing it with the obvious properties of after-discharge and temporal summation, they assign "memory" to it. We remember things, they say, because a reverberating loop gets going and does not stop. They compute, too, that we have enough billion loops in our brain to take care of all the memories we could possibly file away in a lifetime. Perhaps in the end our memory is not just a matter of reverberation but rather one of change in chemical molecules of the neurons around the circuit. Even if that is the case, the loop is essential to memory because its constant activity brings about the chemical change.

Besides memory, the cyberneticists say these loops endow us with 'purpose,' 'will,' motor coordination, and even sometimes with neurosis. At least we can find analogues in electrical instruments and computing machines for such aspects of behavior. In every case the important feature of the loop is *feed-*

back—which means that the events in a loop can feed back to the point where they started and affect themselves. Such feedback can be either negative or positive.

Negative Feedback. In negative feedback, a loop has some natural or prearranged state of activity. Whenever the events in the loop depart from that state, they check themselves through feedback. When you set the volume control of your automobile radio, for example, the loudness of the radio stays the same (within limits) even though you get nearer or farther away from the radio station. It does that because there is a negative feed-back circuit in the radio. There is a loop from the output of the radio back to its input. When the output gets too loud it cuts down the "gain," *i.e.*, the amount to which the radio signal is amplified. When the output is too weak it "opens up" the amplifier to give you a louder program. This is negative feedback, because the output makes the input do the opposite of what it is doing, and thereby the system gets to, and stays in, a stable state.

Reflexes. This kind of feedback is at work at many levels of function in the body. Take the pupillary reflex, for example. Light falling on the eye reflexly makes the pupil contract. A small pupil, however, cuts down the light getting into the eye so that the opposite sort of reflex occurs, *viz.*, dilation. This, of course, lets more light into the eye and causes the pupil to contract. If this loop of negative feedback took place in steps as we describe them, our pupils would be widening and contracting all the time. Actually the loop is at work all the time, and thus the reflex gets to a steady state and stays there within a short time after the stimulus for the eye is presented or taken away.

Hunting. Negative feedback not only accounts for steady states of this sort but also for cases of 'hunting' and 'purposeful movement.' Gun directors used in the last war and automatic missiles that hunt out and home on a target without any human direction are just two examples of such negative feedback. Each of these instruments reacts to a stimulus. When the stimulus is off the center of their 'eyes,' the loop inside them makes them turn toward the stimulus. The more they point toward the stimulus, the less the feedback forcing them to point to it. When they are pointed directly toward it they have found their target and are in a steady state. Then negative feedback is at its lowest point. The principle is the same as in the automatic volume control of the radio.

Coordination. Various sorts of motor coordination and motivated behavior can be described in the same way. We see an object out of the corner of our eye, and feed-back circuits in our brain start our eyes turning toward the object. As our eyes move, the object gets closer and closer to the center of our retina, and this cuts down the feedback turning our eyes. Because of the loop made by our eyes, the nervous system, and the stimulus, we turn to the object and stop with our eyes on it. This is only one example. Almost any case of motor coordination could be cast in the same terms.

Purpose. We can think even of motivation, purpose, and will as the outcome of loops in which there is negative feedback. When we are motivated, our 'automatic volume control' has gone off center. The drive conditions within our body start us doing something which ends up in eating, drinking, or the like. Such eating or drinking directly or indirectly changes the drive state in our body, cutting down (by negative feedback) our actions to 'satisfy' the drive. Thus, for example, we have a loop made up of drive, behavior, and food that is closed and has negative feedback in it. This kind of analogy can be made not only for motivation but also for its relatives, such as purposeful behavior, goal seeking, and 'volition.' It takes only a little imagination to extend such notions to almost any example one wants to dream up.

Positive Feedback. A second kind of feedback also gives us some clever analogies. In positive feedback we have a 'vicious circle.' The output, instead of making the input do the opposite of what it is doing, makes it do the same thing. Thus if the output increases, it affects the input to make the output increase still more. Or if the output decreases, it makes the input decrease all the more. In brief, a positive feedback is a situation in which the "more we get, the more we want" and "the more we want, the more we get."

Negative feedback keeps us in a steady state—it keeps bringing us back to normal. Positive feedback, once started, however, takes us further and further away from a steady state and at a greater and greater rate. You can see that this sort of feedback is usually bad whether you find it in men or machines. In fact, because it cannot go on forever, such feedback usually wrecks the machine. When machines go into positive feedback, as they sometimes do, they go "berserk." The only way to stop them is to pull the power switch off, if you can, or wreck the machine.

Much the same thing can be said about people. Neurotic behavior can be likened to positive feedback. Something happens in the loops to change them from a normal negative feedback to a positive feedback. The loops then keep on going, getting more and more active, sweeping other loops into their orbit. If not stopped in some way or other they may take over so much of the organism that we have a first-class psychoneurosis on our hands. Obsessions, compulsive behavior, and floating anxieties, which mark the neurotic person, are all analogous to positive feed-back circuits that have been started and have not been stopped. Cyberneticists suggest that therapy by convulsive shocks or by cutting some of the pathways of the brain sometimes helps neurotics because it breaks up the positive feed-back circuits, it "clears the machine" and lets it start over again on negative feed-back principles of operation.

The Brain as a Television Set. The cyberneticists have many ideas—enough, in fact, to fill a book (see Wiener)—but we have time for only one more. This is an analogy of the brain to a television system. In television, pictures are transmitted from one place to another because they are electrically broken up into a code. What happens, in effect, is that a very small beam scans the picture at a very rapid rate, just as we might read the page of a book. It runs across a line, then sweeps back to scan another line, then the next line, and so on. This scanning goes on hundreds of times a second. The beam codes what it "sees" as it goes along into a series of signals that are put on the radio carrier waves and broadcast over the air. The television receiver at home is a device for decoding the television signals; by scanning the picture tube, it puts on the tube the picture that originated in the television station. It is interesting that the television receiver may be anywhere in the vicinity, so long as it can pick up the radio carrier wave, and still decode and reproduce the picture.

Cyberneticists suggest that the nervous system works like a television system (Wiener; Walter and Walter). The alpha wave, which seems to be the normal rhythm of the brain, could serve as a scanning and carrier wave. This wave could pick up "the picture" coming into the brain from the various sensory pathways, code it much as television signals are coded, then carry the signals to different parts of the cortex for decoding. The rate of scan, about 10 per second, is rather slow for a television system, but it certainly is fast enough for what the brain does. Any of the cortical areas might then act as television receivers by decoding the signals carried on the alpha waves. Such a scheme, cyberneticists point out, might solve many of the perplexing problems of equipotentiality and recovery of function in different cortical areas.

Comment. We have given you some of the high lights of cybernetics. There are many more detailed notions in the articles and books being published on the subject. As we said at the outset, these ideas are mainly analogies between the brain and electrical concepts. As such they prove nothing at all about the brain. Indeed, the brain may have little or nothing in common with the way we design electrical instruments or computing machines. On the other hand, it may. At the very least the ideas are interesting and stimulating; at best, they may some day be very helpful in giving us new facts and a new understanding of how the body functions in behavior.

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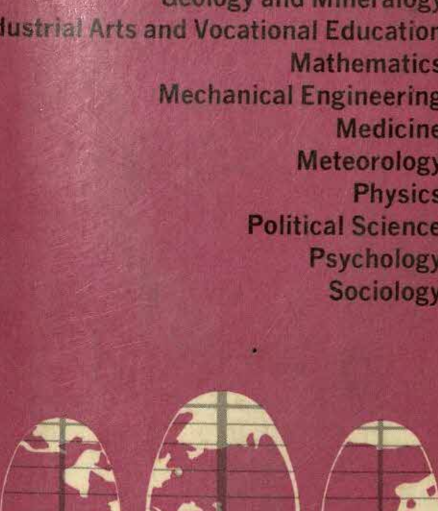

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